CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS

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I hereby declare that the thesis entitled "**CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS**" submitted towards partial fulfillment of the requirements for the award of **MD in PATHOLOGY** degree to BFUHS is a compilation of original work carried out by me under the supervision of **Dr. Pavneet Kaur Selhi**, Professor, Department of Pathology, **Dr. Ruchita Tyagi**, Assistant Professor, Department of Pathology and **Dr Ramit Mahajan**, Associate Professor, Department of Gastroenetrology. No part of this thesis has formed the basis for the award of any degree previously.

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Dedicated

to

my Family

&

Teachers

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*"**As we express our gratitude, we must never forget that the highest appreciation is not to utter words, but to live by them**."*

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LIST OF ABBREVIATIONS

AFB	Acid Fast Bacilli
CA125	Cancer antigen 125
CA 19-9	Carbohydrate antigen 19-9
CT	Computed tomography
DAB	Diaminobenzidine
DPX	Distyenedibutyl phthalate xylene
EUS	Endoscopic ultrasound
FNA	Fine needle aspiration
FNAC	Fine needle aspiration cytology
H&E	Hematoxylin & eosin
IHC	Immunohistochemistry
MGG	May Greenwald Giemsa
MRI	Magnetic Resonance imaging
PAP	Papanicolaou stain
PAS	Periodic acid Schiff stain
PBS	Phosphate buffered saline
USG	Ultra sonography
ZN	Ziehl Neelson

ABSTRACT

Introduction: Pancreatic masses are a common cause of morbidity and mortality with non specific symptons. Pancreatic lesions are divided into benign and malignant. Management can be medical or surgical depending upon the site of involvement and etiology. As pancreas is a retroperitoneal organ, image guided FNAC has been increasingly utilized as a minimally invasive first line procedure for the diagnosis.

Aims & Objectives: To analyze cytomorphological features of pancreatic lesions and classify them according to Papanicolaou Society of Cytopathology System for reporting Pancreaticobiliary Cytology.

Material & Methods: Fine needle aspiration smears from pancreatic masses received in Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 2 years from 1st March 2020 to 28th February 2022 will be analyzed.

Results: A total of 70 pancreatic FNA cases were analyzed. 51-60 years of age group was most commonly involved. Mean age was 60.14 years with male to female ratio of 2.5:1. Adenocarcinoma was the most common diagnosis made on cytology with non diagnostic being the least reported category.

Conclusion: In every patient, personal history, clinical, biochemical and radiological findings were recorded. The youngest patient was 10 years old and eldest was 88 years. Pancreatic head was the most commonly involved site with uncinate process being the least involved site of pancreatic lesions. Positive or malignant was the most common involved category with adenocarcinoma being the most common reported diagnosis. Pain abdomen was the most common presenting complaint. Most of the patients underwent USG guided FNAC. Histo-cytological correlation was done wherever possible and chronic pancreatitis was most misinterpreted lesion in our study. Positive predictive value was 94.5%.

Keywords: Pancreatic, FNAC, Neoplastic, Papanicolaou, Malignant

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INTRODUCTION

Pancreas is a retroperitoneal organ with its head situated in the loop of duodenum and reaching up to hilum of spleen. Pancreatic lesions are divided into benign and malignant. Among benign, the most common presentation is of acute and chronic pancreatitis and amongst malignant lesion, is mostly adenocarcinoma of pancreas. Pancreatic lesions both benign and malignant are a significant cause of morbidity and mortality. Malignant lesion mainly adenocarcinoma of pancreas has become the third leading cause of death among cancers.[1] Hence the early detection and proper treatment whether it is medical treatment or surgical treatment for both benign and malignant lesions is of prime importance. This poor survival rate is mainly due to late clinical presentation, nonspecific signs and symptoms and other major drawbacks like limited diagnostics and limited therapeutic modalities.[2] Accurate diagnosis of pancreatic lesions whether benign or malignant is important for improving the efficacy of the therapeutic interventions.[3] Pre-operative diagnosis of pancreatic masses is a challenging task owing to the non-specific clinico-radiological signs and technical difficulty in performing FNAC. FNAC can be performed by a gastroenterologist by endoscopic technique or by an interventional radiologist under CT/USG guidance.[4] After performing FNAC, adequacy of the sample is checked by rapid on site evaluation so that proper outcome and diagnosis can be made by a cytopathologist. Benign lesions can be managed medically with proper follow ups whereas malignant lesions can be treated surgically. With the advent of advanced imaging techniques and guided FNA, cytology has emerged as a major tool for diagnosing pancreatic lesions, though surgical pathology is often considered to be the gold standard for diagnosis.[5] Endoscopic ultrasound-directed fine-needle aspiration is a minimally invasive technique for the biopsy of pancreatic cysts and mass lesions. It allows the easy and adequate sampling of the tissue with minimal post procedural effects. It also allows the rapid onset evaluation to look for the adequacy of the material being aspirated.[6] The technique is

associated with low morbidity and high diagnostic accuracy. Interpretation of cytologic material obtained from the pancreas is a challenging task due to many infectious diseases as well as benign and malignant neoplasms arising from the pancreas.[7] The cytologic appearances of a majority of pancreatic neoplasms are of specific presentation, allowing precise recognition of the type of neoplasm present. Whereas separation of neuroendocrine, acinar, and ductal neoplasms is usually straightforward but the greatest diagnostic challenge in pancreatic fine-needle aspiration is the to distinguish between atypical epithelium secondary to chronic pancreatitis from well-differentiated ductal adenocarcinoma.[8] Also a number of in situ lesions have been identified recently which lead to complications in diagnosing pancreatic neoplasia on the basis of cytology which includes pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasm.[9]

Moreover, FNAC of pancreatic masses allows for rapid on-site evaluation and triaging of material for ancillary studies. FNAC is a time saving, minimally invasive and well tolerated diagnostic modality which can be done as an out patient procedure to reach definitive diagnosis.[3] Aspiration cytology and histology of pancreatic lesions together can provide a definitive diagnosis. Fine needle aspiration cytology (FNAC) can be done either under USG guidance or endoscopically and allows us to get samples not only for cytological evaluation but also for triaging material for ancillary studies such as flow cytometry, immunohistochemistry and molecular studies.[3]

Percutaneous punctures, USG and CT-guided approach for Fine needle aspiration has its own limitations as pancreas is a retroperitoneal organ which makes it probably inaccessible to reach and has close proximity to the other vital organs, therefore Endoscopic ultrasonography guided FNA is relatively safer and has low risk, leading to accuracy of the tissue biopsy. Endoscopic ultrasonography (EUS) is an indispensable tool for diagnosing both solid and cystic pancreatic lesions.[10]

It has gained widespread acceptance among clinicians and patients. It provides useful information such as differentiating a neoplastic lesion from a non neoplastic one and further recognizing the lesion as benign or malignant. In this study, we have studied the entire spectrum of pancreatic lesions diagnosed on fine needle aspiration (FNA), which will throw light on pattern of lesions observed and has been categorized according to the Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.[11]

AIMS AND OBJECTIVES

To analyze cytomorphological features of pancreatic lesions and classify them according to Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.

REVIEW OF LITERATURE

Pancreas is a transversely oriented retroperitoneal structure extending from the C-loop of the duodenum to the hilum of spleen.[1] It is a complex lobulated organ with distinct exocrine and endocrine components. The majority of the pancreatic parenchyma is composed of exocrine part constituting 80-85% of the organ and is seen as acinar cells. Endocrine part constitutes of 10-15% of the pancreatic parenchyma which is composed of islets of Langerhans. Islets consist of four major cell types- beta, alpha, delta and PP cells (pancreatic polypeptides).[1]

Cytology of normal pancreas:

Pancreas is composed of acinar cells, ductal cells and islets of Langerhans.

Acinar cells: It is the most predominant cell type. These cells have pyramidal to triangular shape with abundant granular cytoplasm, round to eccentric or central nuclei and fine chromatin with often distinct nucleoli.[12] These cells stain trypsin positive.

Ductal cells: They are seen as two dimensional flat sheets with 'honeycomb' appearance having 'picket fence arrangement' with basally located nuclei. These cells have cuboidal to columnar shape with scant, pale cytoplasm and bland appearing nuclei.[12] These cells stain CK7 and CK19.

Embryology of pancreas: Derived from foregut, pancreas develops from two buds. Ventral bud, arises from hepatic diverticulum and gives rise to main pancreatic duct and uncinate process of pancreas. Dorsal bud, arises from dorsal aspect of the duodenum and gives rise to the body, isthmus ,tail of pancreas and accessory pancreatic duct.[13]

Both the ventral and dorsal buds contribute to pancreatic head.

Abnormalities during embryogenesis can lead to 4 conditions

1- Annular pancreas- This condition is due to abnormal rotation of the ventral pancreatic bud forming a ring of pancreatic tissue which encircles 2nd part of duodenum leading to duodenal narrowing. Patients mainly present with bilious vomiting. [1]

2- Pancreatic divisum- This common condition occurs when there is failure of fusion of dorsal and ventral buds at 8th week. Patients present with chronic abdominal pain and/or pancreatitis.[1]
3- Ectopic pancreas- It is usually an incidental finding in which normal looking pancreatic acini are situated at sites other than normal pancreas mainly stomach, duodenum, jejunum followed by Meckel's diverticula and ileum.
4- Agenesis- It is associated with germline homozygous mutation of PDX1 gene encoding a homobox transcription factor critical for development of pancreas.[14] It is a lethal anomaly in which patients often presents with diabetes.[15]

Presentation

Patients with pancreatic lesions mainly present with pain in abdomen radiating to back which can be associated with nausea, vomiting and increase in serum amylase and lipase levels. Sensitivity of lipase is higher than amylase in diagnosing inflammatory lesions of pancreas though definitive diagnosis of any pancreatic lesion is through the FNA and biopsy.[1] Serum calcium levels plays an important role by differentiating hypercalcemia induced pancreatitis or gall stones induced pancreatitis. Similarly serum cholesterol and triglyceride levels have a significant importance in pancreatic pathology.[1]

Tumor markers like CEA and CA19-9 also plays an important role in determining the type of lesion. Levels of tumor markers helps in accessing the type of lesion whether it is neoplastic or non-neoplastic. Markedly increased levels of these tumor markers let the clinician think of a malignant process with low levels can be seen in non-neoplastic conditions.

Due to its retroperitoneal site, the imaging techniques are often required to guide the biopsy needle to sample the target area.[16] Although clinical presentation, radiological findings and location of pancreatic mass is helpful, but tissue diagnosis remains the gold standard for final diagnosis and to plan the management.[16] As the patient presents with signs and symptoms representing pancreatic

pathology with deranged amylase and lipase, CT scan, USG or MRCP plays really crucial role in accessing the type of lesion, site of lesion and its extent. It helps in determining the underlying condition of main pancreatic duct whether it is dilated or normal. Dilated main pancreatic duct is usually seen in pancreatic malignancy with patient presenting with jaundice.[17] It also helps in distinguishing cystic lesions from mass lesions. Imaging modalities used for pancreatic FNA are Ultrasound guided and Endoscopic USG guided. Endoscopic USG guided FNA allows continuous, real time visualization of a needle as it punctures its target lesion.[18] It has better ability to sample small lesions and can have better access to detect vascular and nodal involvement. The diagnostic efficacy and accuracy of EUS guided FNA depends mainly on sample adequacy, lesion characteristics, endoscopy operator and cytopathology expertise.[19] Ultrasound guided FNA also allows sampling of the lesion in real time but visualization can be impaired by bowel and fat. Computed tomography (CT) has better visualization but does not allow real time identification of the needle tip during sampling. Multiple sections of CT has to be taken during sampling of pancreatic lesion which is time consuming and makes it difficult for patient to undergo the procedure.

FNA of a pancreatic mass is performed after imaging has defined site, dimensions, anatomic relationships, depth and solid or cystic nature. The nature of a pancreatic mass needs to be ascertained in order to plan correct therapy; therefore, intraoperative study of the lesion is necessary when preoperative tests do not yield satisfactory results. Classic intraoperative biopsy, which has been used for some time, can cause complications, such as fistulae, abscesses and protracted bleeding. In contrast, FNA is useful due to its high sensitivity and specificity and lack of complications, and intraoperative cytology has proven to be a valuable tool in the diagnosis of pancreatic lesions.[20]

Distinction between neoplastic (benign and malignant) and inflammatory lesion is vital for patient management. The increasing use of radiological techniques has led to the identification of relatively small

lesions, which can be accurately sampled with the help of image guidance.[21]

The benefit of FNAC is simplicity of the procedure as it is less invasive and associated with fewer complications. It involves the use of endoscopic ultrasound in which an echoendoscope is placed into the stomach or duodenum and by the use of ultrasound transducer on the tip of echoendoscope, a small gauge needle is passed into the lesion. FNA can be done through transgastric route if the lesion is in pancreatic tail or body as they are close to stomach bed, or through transduodenal route if the lesion is in the pancreatic head.[21]

Endoscopic ultrasound—guided fine-needle aspiration (EUS-FNA) is first-line procedure in diagnosing the solid pancreatic lesions. Of the broad differential diagnosis of solid pancreatic masses including both malignant and benign lesions, the primary ductal adenocarcinoma accounts for atleast 85% of solid pancreatic masses, being the most common of them.[22]

It also helps in diagnosing the cystic lesion of pancreas such as mucinous cystic neoplasm and pseudocyst. Cytology is also useful in diagnosing the non neoplastic lesion such as chronic pancreatitis and lymphoepithelial cyst.[23]

FNAC sometimes has its own limitations to reach a final diagnosis therefore ancillary techniques like cell block technique or histology is useful and improves the efficacy and accuracy of cytological diagnosis.[24] Though cell block technique allows processing of limited amount of cellular material for histopathological analysis, cytochemistry and IHC but they should not be considered diagnostic for reporting pancreatic lesions as they may have limited amount of cellular material for final interpretation .[25] Thus the combination of cytological smears, cell block preparation and histopathological examination with panel of special stains optimizes the utility of FNAC in the diagnosis of pancreatic lesions.[25]

Due to the advances in scientific techniques, molecular studies like gene mutation techniques have also played a major role in evaluating the disease process and helps in knowing the nature of disease and

survival rate of the patients. Tumor markers such as CEA and CA19-9 along with mutation status and gene evaluation like KRAS, BRCA1/2 and SMAD4 also plays an important role in evaluating the disease.[26-27] In case of any cystic lesion, cyst fluid biochemical analysis is useful and the amount of amylase and lipase levels helps in differentiating whether the lesion is probably non neoplastic or neoplastic.[28]

Cytology of Pancreatic Masses-

Aspirates from the pancreas is divided into neoplastic and non neoplastic lesions. Neoplastic lesions are further divided into benign and malignant categories while non neoplastic lesions can be inflammatory or non inflammatory.

Common lesions of pancreas include-

1- Non neoplastic lesions: Pancreatitis (Acute, Subacute and chronic), Pseudocysts and cysts.
2- Neoplastic lesions: Cystadenoma, Pancreatic carcinoma (ductal cell origin and acinar cell origin), cystadenocarcinoma, solid papillary neoplasm, islet cell tumour and metastasis to pancreas.

Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology has divided lesions of pancreas into 6 categories**:[6]**

1. **Non Diagnostic**
2. **Negative for malignancy**

Benign pancreatic tissue
Acute pancreatitis
Chronic pancreatitis
Autoimmune pancreatitis
Pseudocyst
Lymphoepithelial cyst
Spenule/ accessory spleen

3. Atypical

4. Neoplastic

Benign: Serous cystadenoma
Neuroendocrine microadenoma

Lymphangioma

Other: Well differentiated neuroendocrine tumor

Intraductal papillary mucinous neoplasm, all grades of dysplasia

Mucinous cystic neoplasm, all grades of dysplasia

Solid pseudopapillary neoplasm

5-Suspicious (for malignancy)

6- Positive for malignancy

Ductal adenocarcinoma of the pancreas and its variants

Cholangiocarcinoma

Acinar cell carcinoma

Poorly differentiated (small and large cell neuroendocrine carcinoma)

Pancreatoblastoma

Lymphoma

Metastatic malignancy

Non diagnostic

A non-diagnostic cytology specimen means the one which does not provide any useful information to reach diagnosis. A nondiagnostic sample may be an obscuring artifact, gastrointestinal epithelium, normal pancreatic tissue elements or any acellular aspirate.[29] Ancillary testing and imaging characteristic of the lesion is important before labeling the sample as nondiagnostic. Ancillary testing is important for particularly pancreatic cyst especially CEA and amylase levels.[30] Low CEA and amylase levels in cases of pancreatic cyst favors non diagnostic if the aspirate is acellular.[30] It can be also due to presence of contaminants obtained mainly during endoscopic USG guided FNA procedure. Gastric mucosa, bowel mucosa, hepatocytes, blood clots and mesothelial cells are some type of contaminants obtained during pancreatic FNA. Bowel mucosa is usually obtained while doing endoscopic transduodenal procedures while gastric mucosa is obtained during endoscopic transgastric procedure. Before reporting non diagnostic, clinical and imaging information should always be taken into consideration.[31] Presence of normal pancreatic tissue on

FNA without any abnormal cell in setting of clearly visible solid mass like lesion or cystic lesion on imaging should be reported as non-diagnostic. Image based characteristics of the lesion and ancillary testing is important for mainly cystic lesions before labeling as non diagnostic.[32] Cyst fluid analysis and biochemical testing plays a vital role in overall evaluation.

Negative (for malignancy)

Cytological smears which are not containing material indicative of malignancy or any degree of cellular atypia but are adequately cellular are referred as negative.[33]

Aspirate from normal pancreatic tissue can occasionally be cellular. Exocrine epithelial cells are seen in rounded acinar clusters. The ductal epithelial cells form monolayered sheets.

Pancreatitis: Variable number of acute and chronic inflammatory cells admixed with degenerating or regenerating acinar and ductal epithelial cells are seen. Background shows foamy macrophages and cellular debris in mucinous material.

Acute pancreatitis- Most of cases presenting with acute pancreatitis have a history of alcoholism, trauma or snake bite and are treated accordingly without any active intervention. Although FNAC for acute pancreatitis is rarely performed, the smears are cellular with dominance of neutrophils along with fragments of granulation tissue and aggregate of necrotic fat and foamy macrophages.[34] The epithelial component show minimal atypia with mitotic activity restricted to granulation tissue component mainly. This granulation tissue is mainly composed of reactive fibroblasts with endothelial cells and inflammatory infiltrates. Biochemical analysis show raised serum amylase and lipase levels.

Chronic pancreatitis- These patients have obstruction of the ductal system and presents with severe abdominal pain along with features of both endocrine and exocrine dysfunction of pancreatic tissue.[35] Obstruction of ductal system, alcoholism, hyperparathyroidism, hereditary diseases, viral infections and tuberculosis are also the factors leading to development of chronic pancreatitis . Imaging studies

have shown pancreatic parenchymal atrophy with scarring and pancreatic duct dilatation with presence of pancreatic stones. FNA is usually recommended in cases of focal enlargement of pancreatic tissue and to exclude malignancy. Smears are variably cellular with presence of chronic inflammatory infiltrates along with ductal, acinar and islet cell epithelium but acinar cells decreases with late stages.[36] The diagnosis of chronic pancreatitis is made usually on imaging and clinical findings and FNA is not recommended in most of the cases. Biochemical studies show normal to mildly raised levels of amylase and lipase.

FNAC shows presence of chronic inflammatory infiltrates with ductal, acinar and Islet of Langerhans which are atrophied in late stages. There is seen fibrosis with cellular debris and calcification. Loss of normal honeycomb monolayer sheeting pattern with reactive nuclear changes is seen in chronic pancreatitis but there is absence of nuclear atypia. Some cases also show squamous metaplasia.[37]

Autoimmune pancreatitis- It is pathogenically distinct form of chronic pancreatitis related to IgG4 associated diseases. It is a systemic disease associated with sclerosis involving other body sites too including sclerosing mediastinitis, retroperitoneal fibrosis, sclerosing cholangitis, reidel's thyroiditis and sclerosing sialadenitis.[38,39] FNA is usually not done to diagnose autoimmune pancreatitis. If done, cell blocks are often made for confirming the diagnosis which shows tissue fragments with fibrosis and embedded mononuclear inflammatory cells suggesting the diagnosis of autoimmune pancreatitis. Flow cytometric analysis for IgG4 may be useful in confirming the diagnosis.[40] Ductal epithelial cells are few to absent but if present, they show reactive changes and significant atypia. Cell blocks are extremely useful in demonstrating tissue fragments with underlying fibrosis and infiltration by mononuclear inflammatory infiltrates mainly lymphocytes and plasma cells.[41]

Cysts : Cysts in the pancreas can be congenital or post pancreatic pseudocysts. Pseudocyst represent liquefactive necrosis of the pancreatic tissue. These lesions lack an epithelial lining. The aspirates

are cellular with presence of mixed inflammatory cells composed of lymphocytes and histiocytes.[42] There is lack of serous and mucinous cyst wall lining. Crystalline debris, hemosiderin-laden macrophages and calcifications may be seen. These non-neoplastic cysts are the most commonly encountered pancreatic cysts. Being fluid collections occurring in post-pancreatitis states, they are not true cysts and as such are lined by granulation tissue not by epithelium. Aspiration yields copious turbid watery fluid which contains debris, occasional inflammatory cells including histiocytes, possible fibroblasts and bile, and perhaps rare fragments of epithelial tissue from the surrounding gland. Raised enzyme levels and low or absent tumor marker levels are found in the aspirated cyst fluid. The fluid is non mucinous, but may demonstrate background fibrinous strands. If the aspirate appear purulent, it should be submitted for culture to confirm secondary infection.[43]

Some tumors are inherently and primarily cystic; in addition, any neoplasm, benign or malignant, may undergo cystic degeneration. Evaluation of cysts by radiologic or endoscopic features alone can sometimes be problematic.Chemical analysis of pancreatic cyst fluid may be useful in distinguishing benign from neoplastic cysts. In general, with some exceptions, benign cysts contain raised levels of pancreatic enzymes (amylase, lipase, leukocyte esterase), while tumor markers (CEA, CA 125) are raised in malignant cysts.[44] Cytologic evaluation of aspirated cyst fluid is widely used and often fully diagnostic of the nature of the cyst, although sampling and interpretative errors are acknowledged.[44]

Lymphoepithelial cysts appear to be pancreatic homologue for morphologically similar branchial cleft cyst. They are lined by squamous epithelium associated with abundant lymphoid tissue in the wall and are multiloculated. They are seen as abundant anucleated squamous cells with sheets of benign squamous epithelium. Aspirated cyst content is usually thick with presence of cholesterol crystals. Amylase levels are low in it with occasional high CEA levels.[45]

Splenule/ Accessory spleen: It mostly arises in the tail of pancreas with common presentation as of neuroendocrine tumor except they don't have plasmacytoid cytoplasm of neuroendocrine tumor cells.[46] Aspirate is bloody with platelet aggregates dispersed among tissue fragments composed of lymphocytes and endothelial cells. Lymphoglandular bodies are seen.[47]

Atypical

Cases under this category shows a spectrum of architectural and/or cellular changes beyond normal or reactive but quantitatively or qualitatively insufficient for classification as neoplastic or positive for malignancy.[48] The aspirates are cellular with maintained nuclear to cytoplasmic ratio, however individual cell may show slight irregularity of nuclear membranes but marked nuclear clefting and rat bites are not seen.[48]. There is loss of architectural polarity with mild degree of alteration in the honeycomb pattern in the epithelial cell sheets along with nuclear crowding and mild degree of nuclear overlapping. True nuclear moulding is absent with loss of cell balls with marked nuclear overlapping obscuring the nuclei.[49] The cells which show loss of polarity and haphazard arrangement of nuclei is restricted to lower 2/3rd of the cell only, however this is not restricted to the base of cells.[50] There is absence of more than two-fold variability in cell nuclear size and loss of necrosis. The background may contains RBC or inflammatory cells due to a reactive process or it may be clear. There is seen parachromatin clearing in atypical smears but no drunk honeycomb pattern or marked anisonucleosis (4:1) is noted. Nucleoli may be prominent but there is absence of macronucleoli.

This is an indeterminate category containing spectrum of lesions ranging from benign showing mild degree of nuclear enlargement, hyperchromasia and anisonucleosis to smears showing features which are failing to fall in category of suspicious or malignant. The features of atypical smears are more towards benign disease. The risk of malignancy for atypical category is high that is upto 45 to 65%. There is also noted some variability on the basis of cytological sampling, type of lesion and site of lesion and procedural type.

Neoplastic: Benign

The neoplasm can be cystic or solid, while others can be benign or malignant. The endocrine tumors of pancreas are rare in comparison with tumors of exocrine pancreas, accounting for only 2% of all pancreatic lesions.[51] Pancreatic cystic lesions comprise a vast group of lesions which posses varying degrees of malignancy out of which majority are pseudocysts and other are mucinous neoplasms which includes cystadenomas, mucinous cystadenocarcinomas, intraductal papillary mucinous neoplasms or serous cystadenoma. Majority of tumors are seen in the head of the pancreas. The 5 year survival rate of pancreatic tumors is 10%.[52] As FNA is a minimally invasive technique, it helps investigators to get cyst fluid for biochemical and cytological evaluation.[53]

Serous Cystadenoma (Microcyst / Glycogen Rich Adenoma): Aspirate is clear and watery, some are acellular, while others contain a sparse exfoliate of monomorphic round cells with finely vacuolated, glycogen positive, mucin-negative cytoplasm, and centrally disposed nuclei containing fine chromatin. The cells are cuboidal, non mucinous and are present in small clusters that form flat sheets or small groups. They have round, central to eccentric nuclei with smooth nuclear membranes and evenly dispersed chromatin with indistinct nucleoli.[54] No necrosis, atypia or mitosis is evident in these smears. They contain fine fibrous septa surrounded by cuboidal, glycogen rich cells without cellular atypia. These cystadenomas have a very delicate lining which gets disrupted while procedure and results in bloody aspirate.[55] Therefore they often result in non diagnostic report as they lack epithelial cells. Occasionally, larger monolayered sheets may be obtained. The cell groups may resemble mesothelial cells or bland acinar cells. Cell blocks are usually made to make diagnosis of serous cystadenoma as the cyst lining is very delicate to withstand the mechanical forces of smearing. Liquid based processing or cytospin preparations of cyst fluid are better as they yield epithelial cells. The epithelial cells are bland, cuboidal and non mucinous with fine vacuolization.[56] The

fibrous septas are highly vascularized. As the smears are highly vascular, there may be abundance of hemosiderin laden macrophages. Endoscopic USG guided procedures are better as they yield more number of cells for cell blocks.[56] Intracytoplasmic glycogen can be confirmed by special stains for periodic acid Schiff (PAS) and PAS with diastase. Immunohistochemical markers like alpha-inhibin and GLUT1 are specific for serous cystadenoma. CEA and amylase levels are low.

Neuroendocrine microadenoma: They are also known as islet cell tumor-lets.[57] They are small in size with less than 5mm of diameter in greatest dimension.[58] They are typically identified on imaging and cytological correlation is essential for its diagnosis.

Lymphangioma: These are very rare neoplasms accounting for less than 0.2% of all pancreatic lesions. On imaging they appear as large solitary or multicystic hypoechoic lesions with no connections to main pancreatic duct.[59] Aspirates are non mucoid, yellow and water cyst fluid. There are numerous small mature appearing lymphocytes, however no epithelial cells are seen in the background. CEA and CA 19-9 levels are low. Amylase levels are mildly elevated.[59]

Neoplastic: Others

These lesions are either preinvasive or premalignant such as intraductal papillary mucinous neoplasm or mucinous cystic neoplasm with low, intermediate or high grade dysplasia. Also included in this category are pancreatic neuroendocrine tumors and solid pseudopapillary neoplasm. The presence of mucinous epithelium represent a neoplastic change.

Pancreatic neuroendocrine tumor: These are usually more than 0.5cm in diameter, however the size of tumor, cytological atypia and degree of hormone production do not correlate with biological behavior.[60] Aspirates are rich in pancreatic parenchyma and poor in stromal tissue with moderate to highly cellularity though scant cellularity is common with cystic degeneration. They are composed of uniform population of mostly dyscohesive epithelial cells giving it a solid cellular smear pattern. Majority of the aspirates show non cohesive single cells with or without medium sized rosettes along with bloody background.

Monotonous population of small to medium sized polygonal epithelial cells are seen with uniform and bland nuclei. The cells have round nuclei with coarse stippled and evenly distributed salt and pepper chromatin with scant amount of cytoplasm displacing the nuclei to periphery giving it a plasmacytoid appearance.[61] Nucleoli are usually inconspicuous but are occasionally quite prominent. Necrosis and mitotic figures are usually absent. Confirmatory stains are usually used like synaptophysin and chromogranin to make diagnosis.

Solid Pseudopapillary Neoplasm: It is solid and cystic low grade malignant epithelial neoplasm. These are highly vascular producing rich, pseudopapillary meshwork of blood vessels.[62] Imaging plays an important role in diagnosing it as it shows both solid and cystic component. Aspirate is cellular and is composed of small, uniform cells which are cohesive with branching along with papillary cell clusters. Background may be clean or contains hemorrhagic debris, foamy macrophages and histiocytes along with multinucleated giant cells. Individual cell have small conspicuous nucleoli and are homogenous in appearance. Nuclei is round to oval with smooth borders or slight grooved nuclear margins.[63] Delicate fibrovascular core with myxoid stroma is noted which is usually PAS positive.[64] Cytoplasm is scant to moderate and may contain perinuclear vacuole or intracytoplasmic hyaline globules.

Neoplastic mucinous cyst: Intraductal papillary mucinous neoplasm and mucinous cystic neoplasm are premalignant cyst. They both are mucin producing neoplasms. They may show invasive behavior.[65] They are classified on the basis of degree of cytological atypia and architectural pattern into low, intermediate and high grade dysplasia, preinvasive and invasive carcinomas. More the epithelial component, more it go towards malignancy, however if the interpretation of mucinous cyst is established by cytology and ancillary testing such as CEA levels or KRAS and GNAS mutational analysis and the epithelial component is inadequate to call it malignant then the appropriate category is Neoplastic ‘Others’.[66] Aspirates are thick with colloid like extracellular mucin with inflammatory debris within mucin. CEA levels

are usually high in neoplastic lesions of pancreas.[67]

Low grade mucinous neoplasm are identified on the basis of neoplastic epithelial cells exhibiting low grade atypia seen as single cell or small clusters and flat sheets of bland glandular epithelial cells which is more than 12 micron the duodenal enterocyte with round regular nuclei and evenly dispersed chromatin and inconspicuous to prominent nucleoli.[67] There is seen honeycomb sheet of cells with basally located nuclei and apical cytoplasmic compartment which are indistinguishable from gastric contaminations. Thick and colloid like extracellular mucin with debris and no epithelial cells is a common finding.

High grade mucinous neoplasm display high grade dysplasia but are insufficient for malignancy. They are scant to highly cellular with presence of epithelial cells that have lost the potential to call it a benign process. They are composed of small to large clusters of cells with less than 12 micron the size of duodenal enterocyte. Three dimensional architecture and papillary arrangement supports IPMN.[68] They have high N:C ratio with mild to moderate nuclear membrane irregularities and variable nucleoli. The necrosis may be scant to moderate but not that abundant to call it malignant.

Suspicious (For malignancy)

The smears are called suspicious when only rare cells display sufficient criteria for definitive diagnosis of malignancy along with lack of clinical, imaging and ancillary testing.[69] These are characterized by moderate to severe degrees of architectural disarray manifested by loss of cellular polarity along with nuclear enlargement, moderate increase in nuclear cytoplasmic ratio, moderate coarsening of chromatin, distinct nucleoli and anisonucleosis. Nuclear membranes show irregularity with folding, clefts and notching. There is three to four times variability in the nuclear size in a single group of cells. They may have mucin filled intracytoplasmic vacuoles. Pseudostratification is seen with nuclei located in upper half or 1/3rd of the cytoplasm.[70] Some cases may show fourfold variation in the nuclear size within a single cell group. They have prominent nucleoli but macronucleoli is absent. Less

number of cells with features of malignancy are categorized for suspicious for malignancy. Threefold variation in the nuclear size within any group of cells is characteristic of it. Nuclear moulding is often seen.

Positive for malignancy

Ductal Adenocarcinoma :It is further differentiated into well, moderate and poorly differentiated types. Most of the ductal adenocarcinomas arise from head and uncinate process of pancreas. The patient usually presents with symptoms like abdominal pain, weight loss, jaundice, new onset diabetes mellitus and hypercoagulability. Imaging plays an important role in diagnosing it. Presence of well circumscribed masses with hypoechoic lesion with irregular borders and double duct sign due to dilation of biliary and pancreatic duct is considered as an important finding of pancreatic ductal adenocarcicoma.[71] Almost all adenocarcinomas arising in the pancreas are of ductal origin without unique features permitting absolute distinction from other carcinomas arising in the biliary tree. The characteristic FNA pattern is of crowded monolayered sheets, with moderately tall columnar palisading cells at luminal edges. Smaller aggregates commonly show rounded glandular structures with feathered edges, or three dimensionality, cytoplasmic borders may be very well demarcated in better differentiated forms; in other cases, the monolayered sheets appear syncytial, without characteristic cytoplasmic changes. The diagnosis of malignancy ultimately depends on nuclear features which range from very subtle alterations to overly malignant criteria with decreasing differentiation.[72,73]

Well differentiated adenocarcinoma:- These tumors show typically single predominant cell type mainly ductal cells with presence of small to medium sized sheets of cells with smooth borders. They have low N:C ratio with mild anisonucleosis, mucinous cytoplasm and parachromatin clearing in an uneven ‘drunken honeycomb’ pattern. They are usually arranged in three dimensional fragments with nuclear crowding, loss of polarity, nuclear membrane irregularities with cleft and notches. There is lack of prominent nucleoli. Necrosis and mitosis is very uncommon in this type of adenocarcinoma.[74]

Moderately differentiated adenocarcinoma:- They have larger sheets of fragments with presence of more cellular pleomorphism than well differentiated adenocarcinomas. Three dimensional fragments are more crowded in these type of lesions.[75]

Poorly differentiated adenocarcinoma:- Total lack of glandular differentiation makes it poorly differentiated. They exhibit extreme pleomorphism with maximum number of singly scattered large pleomorphic cells and loosely cohesive tissue fragments.[76]

Variants of adenocarcinoma:- These includes

- Colloid carcinoma
- Undifferentiated carcinoma with Osteoclastic like giant cells
- Undifferentiated carcinoma
- Adenosquamous carcinoma
- Acinar cell carcinoma

Poorly differentiated Neuroendocrine carcinoma (Small cell or Large cell Neuroendocrine carcinoma):- Small cell neuroendocrine carcinoma resembles small cell carcinoma of lung with small cells having high N:C ratio with presence of nuclear moulding and scant amount of cytoplasm. Apoptotic debris is evident in this type of tumor. However, large cell neuroendocrine carcinoma have cells with abundant cytoplasm.[77]

Pancreatoblastoma: These are unusual, large pancreatic primary tumors encountered in children and adolescents. They demonstrate solid and acinar architecture with interspersed squamous corpuscles, osseous and/or chondroid metaplasia. Smears are cellular and are composed of detached small cells, primitive blastemal epithelial cells with even chromatin and delicate cytoplasm, rare squamous corpuscles and mesenchymal fragments.[78] Cytologic reports of other pancreatic lesions including islet cell tumors have also seen reported in literature and their incidence is low and cytologic diagnostic criteria are not well established.

Lymphoma: Lymphomas mostly occurs in head region of the pancreas. Most common lymphoma is Non Hodgkin’s lymphoma-Diffuse large B

cell type. Aspirates are composed of atypical lymphoid cells in a background of lymphoglandular bodies.[79]

Nishith N et al. studied 581 pancreatic FNA over a period of 12 years from 2008 to 2019 and categorized them according to Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary Cytology and assessed the risk of malignancy for each category. The cytologic diagnoses included 50 nondiagnostic (category I), 175 negative for malignancy (category II), 19 atypical (category III), 27 neoplastic:benign (category IVA), 30 neoplastic:other (category IVB), 26 suspicious (category V), and 254 malignant (category VI) cases. ROM for non-diagnostic aspirates, nonneoplastic benign specimens, atypical cases, neoplastic:benign, neoplastic:other, suspicious for malignancy, and the malignant category was 16.7%, 7.1%, 33.3%, 0.0%, 20.0%, 100%, and 78.6%, respectively [80].

Mancera MS et al. performed a retrospective search for 297 pancreatic FNA cases in 10 years from 2010 to 2019 and found that 30 were nondiagnostic (category I), 45 were negative for malignancy (II), 20 atypical (III), 42 were neoplastic: other (IVB), 19 were suspicious for malignancy (V), and 141 were malignant (VI). The absolute ROM was 10% for category I, 8.9% for category II, 60% for category III, 4.8% for category IV when the neoplasms were not characterized as malignant, and 100% when categorized as malignant; 100% for category V, and 95.7% for category VI. Sensitivity, specificity, positive predictive value, and negative predictive value for neoplasia and malignancy, including categories IV to VI, were 96.6%, 88.4%, 97.5%, and 84.4%, respectively[81].

Sung S et al. studied 1017 cases of pancreatic FNA over a period of 3 years (2014-2017). The cytopathologic diagnoses included 242 nondiagnostic (category I), 162 negative for malignancy (category II), 142 atypical (category III), 20 neoplastic-benign (category IV: benign), 133 neoplastic-other (category IV: other), 28 suspicious (category V), and 290 malignant (category VI) cases. Majority of the patients were female with male to female ratio of 1:1.6. Age ranged from 15 to 95 years with median age of 67 years[82].

Hoda RS et al. studied 322 patients who had undergone pancreatic FNA over a period of 1 years from January 2016 to December 2016. The study cohort included 168 men (52.2%) and 154 women (47.8%). The patient's age ranged from 18 to 91 years (mean, 66.1 years; median, 68 years). Of the 334 pancreatic lesions, 171 (51.2%) were cystic and 163 (48.8%) were solid. Pancreatic masses were found more commonly within the head (n = 139; 41.6%), tail (n = 79; 23.7%), and body (n = 74; 22.2%). Less commonly, the lesions were found in the neck (n = 19; 5.7%), uncinate (n = 2.7%), peripancreatic area (n = 8; 2.4%) and main duct, not otherwise specified (n = 6; 1.8%). The median clinical follow-up time was 18 months (mean, 15 months) [83].

Ilyas AM et al. studied 60 cases of pancreatic FNA over the period of two and half years (2017-2019). These cases were reported according to papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology. His study had comparable results with sensitivity, specificity, PPV, NPV of 92.8 %, 100%, 100% and 92.59% respectively. Risk of malignancy is lower for benign and intermediate category whereas it was higher for suspicious and malignant categories. The average range of patient's ages 45-55 years with an average age of patient being 51 years. There was male predominance with male to female ratio of 2:1. Head of the pancreas was the most common site comprising 48% of all cases followed by body with 40% and last was tail with 12% cases. Out of 60 cases maximum cases [n=19] were reported as malignant comprising 31.60% followed by negative for malignancy [n=16, 26.60%]. Neoplastic category had 9 cases [15.00%], 8 cases were reported as suspicious [13.30%] and 7 cases were non diagnostic [11.60%]. Only 1 case was reported as atypical [1.60%][84].

Eloubeidi MA et al. studied EUS-FNAB of 101 patients (mean age, 62+/- 11.8 years; age range,34-89 years). The male to female ration was 2:1. Sixty seven percent of the lesions were located in the head of the pancreas, 12% were located in the uncinate process, 17% were located in the body and 6% were located in the tail. 64 cases were interpreted as malignant on cytological evaluation, 5 cases were

diagnosed as suspicious, 6 cases as atypical and 26 cases are benign process. Out of 64 malignant cases, 59 were adenocarcinomas, 2 were neuroendocrine tumors, 1 was lymphoma and 1 was metastatic renal cell carcinoma. All except one of the suspicious aspirate were subsequently confirmed to be malignant[85].

Afify AM et al. studied 69 FNAB of pancreatic lesions over the period of 5 years. The patients comprised of 38 females and 31 males with mean age of 65 years. The cytological diagnoses includes 31 malignant, 8 suspicious, 6 atypical, 20 benign and 4 nondiagnostic. Forty three cases were true positive, 9 were true negative, 2 were false positive and 11 were false negative. The overall sensitivity was 80% and specificity was 82%[86].

Layfield LJ et al. studied 317 FNA cases from pancreas over a period of 10 years. The types of samples were solid and cystic. Out of 317, 14 (4.4%) cases were reported as non diagnostic, 103 (32.5%) were negative for malignancy. Atypical smears were 23 (7.2%) in number. None of the case was reported as Neoplastic:Others while 14 cases (4.4%) were Neoplastic:Benign. 22 (6.9%) cases were Suspicious for malignancy and 141 cases (44.5%) were reported as Positive or Malignant[87].

In a retrospective study by **Hank M et al.** ,studied 223 pancreatic FNA cases over a period of 2 years, 115 were females and 108 were males. The age ranges from 18-88 years with a median age of 64 years. Out of 223 cases, 109 (48.87%) cytology smears were from head of pancreas, however 58 (26.00%) were from body, 43 (19.28%) were from tail and 13 (5.8%) were from uncinate process of pancreas. 50 (22.4%) cases were reported as non diagnostic due to insufficient cellularity, 43 (19.28%)were negative for malignancy , 14 (6.2%) were reported as atypical, 12 as neoplastic :benign (5.38%), 55 (24.66%)as neoplastic :others, 15 (6.72%) were reported as suspicious and 34 (15.24%) were malignant. The sensitivity, specificity and accuracy of cytology was 92.5%, 100% and 95% respectively[88].

Wright PK et al. studied 120 EUS-FNA pancreas specimens from 111 patients, of which 112 (93.3%) specimens had follow-up data. There

were 79 and 41 EUS-FNA pancreas specimens from solid and cystic lesions, respectively. Based on the cytology diagnosis the specimens were classified as Panc 1 (non diagnostic) (7.5% n=9), Panc 2 (negative for malignancy) (33.3% n=40), Panc 3 (atypical) (2.5% n=3), Panc 4B (neoplastic; benign) (2.5% n=3), Panc 4O (neoplastic; others) (15.0% n=18), Panc 5 (suspicious) (3.3% n=4) and Panc 6 (positive or malignant) (35.9% n=43). The performance indicators for diagnosis of malignancy or neoplasia with malignant potential, included sensitivity (95.4%), specificity (100%), positive predictive value (100%), negative predictive value (92.3%), false positive rate (0%) and false negative rate (4.6%). Out of 111 patients 52 (46.84%) were males and 59 (53.15%)were females. The range of age of patients was 22-83 years with mean age of 63 years. Maximum patients presented with lesion in the head region of pancreas comprising 42.5% (n=51). 34 (28.33%) patients had lesion in body of pancreas while 17 (14.16%) had in uncinate process and 18 (15.00%) were from tail of pancreas[89].

MATERIALS AND METHODS

SOURCE OF DATA

Fine needle aspiration smears from pancreatic masses received in Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 2 years (one year prospective and one year retrospective, that is 1st March 2020 to 28th February 2022) will be analyzed.

STATISTICAL ANALYSIS

Data was described in terms of range; mean +/- standard deviation (SD), frequencies (number of cases) and relative frequencies (percentages) as appropriate. Risk of malignancy and positive predictive value were calculated. All the statistical calculations were done using (Statistical package for Social Science) SPSS 21version (SPSS iInc., Chicago, IL, USA) statistical program for Microsoft Windows.

METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

FNAC samples from pancreatic masses received in the Cytology Laboratory of the Pathology Department which will include.

1- FNAC slides received after guided aspiration (USG/CT or endoscopic ultrasonography).

2- Prepared and stained slides for review from outside centre.

EXCLUSION CRITERIA

Samples obtained from lesions other than pancreas.

PROCEDURE

After informed consent, radiologically and EUS guided FNAC will be done using 23 gauge needle attached to 20cc disposable plastic syringe under aseptic conditions. Under the radiological guidance, aspiration will be performed and slides will be prepared immediately. One of the slide will be utilized for rapid on the site evaluation for adequacy of the sample received after staining with Toulidine Blue. Two slides will be wet fixed in 95% ethanol for Papanicolaou stain and Hematoxylin and Eosin stain. The remaining smears will be air dried

and stained by May Grunwald Geimsa stain. FNA samples collected in separate pass will be fixed in 10% formalin, processed and embedded to make cell blocks. Sections will be stained by H&E stain. Special stains will be done whenever necessary.

METHOD OF COLLECTION OF DATA

After informed consent, USG guided percutaneous fine needle aspiration (FNAC) was done.

MATERIAL USED

1. Cameco's syringe pistol
2. Disposable 20 ml syringe
3. Needle 21G/ 23G
4. Glass slides
5. Spirit swab
6. Dry swab / cotton gauge
7. Disposable gloves
8. Diamond pencil for marking slides
9. FNAC reporting form
10. Tray for carrying slides

PROCEDURE DONE

Radiologically guided percutaneous fine needle aspiration (FNAC) was done using 21 gauge spinal needle for mediastinal masses attached to 20cc disposable plastic syringe. Taking aseptic precautions, needle was introduced in suspended respiration, slides were prepared immediately. One of the slide was utilized for rapid on site evaluation for adequacy by the Toulidine Blue stain. Two of them were wet fixed in 95% ethanol and stained with Papanicolaou stain and Hematoxylin and Eosin. The remaining smears were air dried and stained by May Grunwald Giemsa stain.

FNA sample was collected in a separate pass and fixed in 10% formalin, processed and embedded to make a cell block. Sections were stained by H&E stain. Special stains were done wherever necessary Cytopathological-histopathological correlation was done wherever possible.

The smears obtained by FNA (ultrasound/endoscopic USG guided) of

all pancreatic masses were analyzed in this study and categorized. The cytological findings were correlated with the clinico-radiological profile, histopathological findings, special stains and IHC findings wherever possible.

Staining of smear

1. Dry fixed smears were prepared by air drying and then fixing in methanol followed by staining with Giemsa

2. Wet-fixed smears were prepared by immediately fixing in 95% isopropyl alcohol and stained by H&E and Papanicolaou stain.

Giemsa Stain:

Giemsa stock

Geimsa stain powder 4 gm

Glycerol 250ml

Methanol 250ml

Giemsa working solution

Giemsa 4ml

Distilled water 96ml

Procedure:

1. Smears were air dried and fixed with methanol.

2.Giemsa stain 1 in 10 dilutions (9ml water, 1ml Giemsa stain) was poured over the slides to cover whole of the smear for 10 minutes.

3. Stain was removed and slides washed with distilled water thoroughly and air dried.

4. Mounting in DPX.

Hematoxylin & eosin

Stain solutions: Harris's Hematoxylin

Hematoxylin 2.5 gm

Absolute alcohol 25ml

Potassium alum 50 gm

Distilled water 500 ml

Mercuric oxide 1.25 gm or

Sodium iodate 0.5gm

Glacial acetic acid 20ml

Eosin 1% (commercially available)

95% Ethyl alcohol

Acid alcohol

1% Ammonia

Acetone

Xylene

1) The smears were fixed with 95% rectified spirit or ethyl alcohol and kept for ½ hour.

2) Then ten dips each were given in 80%, 70%, 50% alcohol.

3) Washed in distilled water-10 dips.

4) Harris hematoxylin- 3 mins.

5) Washed in running tap water till excess stain was removed - 1 min.

6) Acid alcohol 0.5% HCl -10 dips.

7) Washed in running tap water- 30 secs.

8) 1% ammonia -3 dips

9) 95% alcohol -10 dips.

10) Eosin - 20 dips

11) Acetone -10 dips

12) Acetone - 10 dips

13) Xylene -10 dips

14) Xylene -10 dips

Papanicolaou Stain requirements

Stain Solutions:

Harris Haematoxylin

Hematoxylin 2.5gm

Distilled water 500ml

Mercuric oxide 1.25 gm or Absolute alcohol 25 ml

Sodium iodate 0.5 gm

Potassium alum 50 gm

Glacial acetic acid 20 ml

Orange G 6

10% aqueous Orange G 50 ML

Alcohol 950 ml

Phosphotungstic acid 15 gm

Eosin alcohol 36

0.5% light green	0.5% Eosin
0.5% Bismarck brown	95% ethyl alcohol
Phosphotungistic acid	Glacial acetic acid
Lithium carbonate	Absolute methanol

Procedure

1) The smears are wet fixed with 95% rectified spirit for half an hour.
2) Then ten dips each were given in 80%, 70%, 50% alcohol.
3) Washed in distilled water.
4) Stained with Harris's haematoxylin 0-3 mins.
5) Washed in running tap water.
6) Given 10 dips in 1% ammonia.
7) Washed in running tap water.
8) Dipped in 95% alcohol-10 dips.
9) Kept in orange- G 6 for 30 secs.
10) Given 10 dips in 95% and repeated again.
11) Kept Eosin Alcohol 36 for 2 mins.
12) Acetone – 10 dips.
13) Again acetone 10 dips.
14) Xylene – 10 dips.
15) Again xylene –10 dips.
16) Mounted slide with DPX.

Ziehl –Neelsen (ZN) stain requirements-

I. Carbol fuschin

Basic fuschin- 0.5 gm
Absolute alcohol-5 ml
5% aqueous phenol-100 ml
Mix well & filter before use.

II. Methylene blue solution (stock)

Methylene blue-1.4 gm
95% Alcohol -100 ml

III. Working methylene blue solution (working)

Methylene blue -10 ml
Tap water-90 ml

IV.20% sulfuric acid

(1% sulphuric acid for Nocardia, 5% for Leprosy, 20% sulphuric acid for Mycobacterium tuberculosis)

Procedure

1. Make a smear and allow it to dry at room temperature.
2. Flood the slide with carbol fuschin and heat gently until the steam is seen rising from the slide. Do not bring to boil.
3. Heat intermittently for 10 mins.
4. Wash well in tap water.
5. Differentiate in acid alcohol (2-5 dips).
6. Flood the slide with 20% sulphuric acid. Leave this until the smear is pale pink in color.
7. Rinse in tap water.
8. Counterstain with methylene blue till smear is pale blue.
9. Rinse in tap water. Grocott's Methamine Silver Stain

Components: Methenamine silver nitrite

Stock solution: Mix 100 ml of 3% methenamine and 5 ml of 5% silver nitrate. Shake well.

Working solution: Mix 25 ml of stock solution with 25ml of distilled water and 2ml of 5% sodium borate. Fast green

Stock solution: dissolve 0.2 gm of fast green in 100 ml 0.2% acetic acid

Working solution: mix 10ml of stock solution with 40 ml of distilled water

4% solution of chromium trioxide

1% solution of sodium bisulfate

0.2% solution of gold chloride

2% solution of sodium thiosulfate

Fixation: 70% ethyl alcohol for 1 minute

50% ethyl alcohol for 1 minute

Staining procedure

1. Give 15 dips in distilled water
2. Pour 5% chromium trioxide for 2 minutes
3. Coplin jar is transferred to 50degree C water bath and kept for 15 minutes
4. Give 15 dips in tap water

5. Pour 1% sodium bisulfate for 30 seconds
6. Wash under running tap water for 15 minutes
7. Give 15 dips in distilled water
8. Give 15 dips in distilled water
9. Give 15 dips in distilled water
10. Give 15 dips in distilled water
11. Pour Methanamine silver solution and keep for 2 minutes (place coplin jar with solution and slides in 43 degree C water bath)
12. Coplin jar is transferred to 58 degree C
13. Give 15 dips in distilled water
14. Give 15 dips in distilled water
15. Give 15 dips in distilled water
16. Give 15 dips in distilled water
17. Give 20 to 30 dips in 0.2% gold chloride
18. Give 15 dips in distilled water
19. Give 15 dips in distilled water
20. Pour 2% sodium thiosulfate for 1 minute
21. Wash under Running tap water for 15 seconds
22. Fast gram for 30 seconds
23. Wash under Running tap water 15 seconds
24. Give 15 dips in distilled water
25. Give 15 dips in distilled water
26. Give 15 dips in 95% ethyl alcohol
27. Give 15 dips in 95% ethyl alcohol
28. Give 15 dips in 95% ethyl alcohol
29. Give 15 dips in absolute ethyl alcohol
30. Give 15 dips in absolute ethyl alcohol
31. Give 15 dips in absolute xylene

PAS Stain (Periodic Acid Schiff Stain)

Components:

1% periodic acid

Schiff reagent

Distilled water 100ml

Basic fuschin 1gm

Sodium metasulphite 2gm

1N HCL 20ml

Activated charcoal 0.3mgm

Sodium metasulphite solution

Stock solution 10% aqueous solution

Working solution 5% of stock solution + 100 ml distilled water

Oxalic acid 0.5 gm

Potassium sulphite 0.5 gm

Distilled water 100 ml

1% acetic acid 100ml Fixation – 70% ethyl alcohol

50% ethyl alcohol

1% hematoxylin

Procedure

1. Give 15 dips in distilled water
2. Pour Periodic acid for 10 minutes
3. Wash under Running tap water for 10 minutes
4. Pour Distilled water for 15 minutes
5. Pour Schiff reagent for 15 minutes
6. Pour Sodium metasulphite 6 minutes
7. Wash under Running tap water for 10 minutes
8. Pour Hematoxylin for 4 minutes
9. Wash under Running tap water for 5 to 10 minutes
10. Wash under Running tap water for 5 minutes
11. Pour Distilled water and keep for 5 minutes
12. Give 15 dips in Distilled water
13. Give 15 dips in 95% ethyl alcohol
14. Give 15 dips in 95% ethyl alcohol
15. Give 15 dips in absolute alcohol
16. Give 15 dips in absolute alcohol
17. Give 15 dips in xylene

Procedure to make cell block

1. A separate pass was given to collect material for making cellblocks.
2. Suck 20 ml of 10% formalin into the syringe immediately.
3. Put the material with formalin into test tube and leave for 6 hours.

4. Centrifuge the material for 5 minutes and wash with phosphate buffered saline (PBS).Repeat it 3 times.

5. Put 100 ml pooled plasma into button and mix it.

6. Add 25-40 ml of thrombin segment.

7. Leave till the clot is formed.

8. Give it for tissue processing.

Immunohistochemistry - standard Strept Avidin Procedure

1. 2-3 mm sections were cut and mounted on Poly L-lysine coated slides.

Slides were dried overnight at 37°C and dewaxed in xylene and hydrated.

2. Sections were put on Poly L-lysine coated slides and incubated at 60°C for 30 min. The temperature was adjusted at 37°C after 30 minutes. The slides were left in incubator for overnight.

3. All slides were dewaxed by heating with spirit lamp.

Xylene 3 changes for 10 minutes

Xylene/ alcohol 1 change for 10 minutes

100% alcohol 1 change for 5 minutes

95% alcohol 1 change for 5 minutes

80% alcohol 1 change for 5 minutes

70% alcohol 1 change for 5 minutes

Finally all slides were rinsed in running tap water.

4. Antigen retrieval procedure - The black box was filled 3/4th with citrate buffer and the slide carrier with slides was placed in it.

5. The black box was placed in microwave for 9 min.

6. Boiling of the solution was observed and the microwave was reset for 6 min and started.

7. The box was removed and cooled in running tap water.

8. Blocking endogenous peroxidase-sections were incubated at Room temperature in 0.3% H_2O_2 in methanol for 30 to 45 minutes and rinsed in running tap water for 5 to 10 minutes, and dipped in distilled water for 1 minute.

9. The slides were placed in Tris buffer (only 1 change for 5 min).

10. Blocking reagent was applied for 5 - 10 min. The excess blocking

reagent was wiped off.

11. Primary antibodies were applied covering the whole tissue and incubated at room temperature for 1 hours.

12. Slides were then washed in Tris buffer for 5 minutes (4 changes).

13. The slides were cleaned with tissue paper.

14. Ultra Vision One HRP Polymer covering the whole tissue was applied and incubated at room temperature for 45 minutes.

15. Washing was done in TBS buffer (Tris buffered saline) for 5 minutes (4changes).

16. One drop of substrate- DAB (3,3-Diaminobenzidine) solution was applied on each slide covering the whole material.

17. lncubated for 10-1 5 min.

18. All slides were washed in deiodinized water.

19. Hematoxylin was applied for few seconds.

20. The slides were put in running tap water.

21. They were allowed to dry and dehydrate in alcohol.

22. Incubated for 2 min and allowed to dry.

23. Mounted in DPX (distyrene dibutyl phthalate xylene).

24. The slides were examined microscopically.

STATISTICAL ANALYSIS

Data were described in terms of range; mean ±standard deviation (± SD), median, frequencies (number of cases) and relative frequencies (percentages) as appropriate. All statistical calculations were done using SPSS (Statistical Package for the Social Science) SPSS 21 version statistical program for Microsoft Windows.

DURATION OF STUDY

Prospective- One year (1st March 2020- 28th February 2021)

Retrospective- One year (1st March 2021 – 28th February 2022)

STUDY DESIGN

This is both retrospective and prospective study.

OUTCOME

The smears obtained by FNAC (USG/CT/EUS guided) of pancreatic masses will be analysed and categorized on the basis of Papanicolaou

society of cytopathology system for reporting pancreaticobiliary cytology.

OBSERVATIONS AND RESULTS

A total of 2265 cases of guided fine needle aspiration cytology (both Ultrasound guided and Endoscopic USG guided) were received in the department of pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 2 years from 1st March 2020 to 28th February 2022 (1 year retrospective and 1 year prospective), out of which 70 were guided FNAC from pancreas. Sample size was limited due to COVID 19 pandemic.

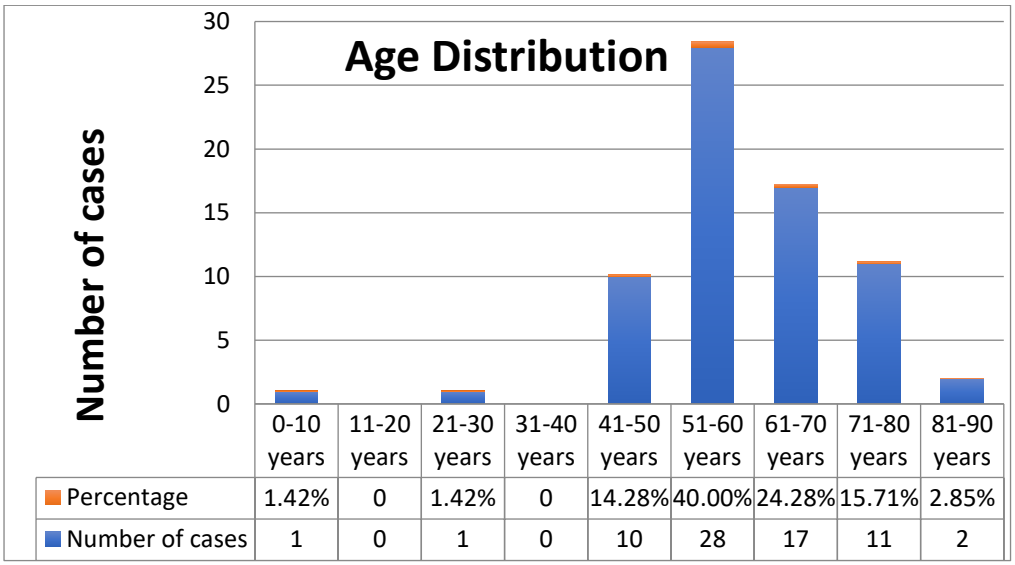
Age Distribution of Patients [n=70]

The commonest age group who underwent fine needle aspiration cytology of pancreatic lesions was 51-60 years comprising of 28 cases [40.00%]. The youngest patient was 10 years old while the eldest patient was 88 years old . Mean age was 60.14 years.

Table 1-Age distribution [n-70]

Age group	Number of cases	Percentage
0-10 years	1	1.42%
11-20 years	0	0%
21-30 years	1	1.42%
31-40 years	0	0%
41-50 years	10	14.28%
51-60 years	28	40.00%
61-70 years	17	24.28%
71-80 years	11	15.71%
81-90 years	2	2.85%

Figure 1-Age distribution [n=70]

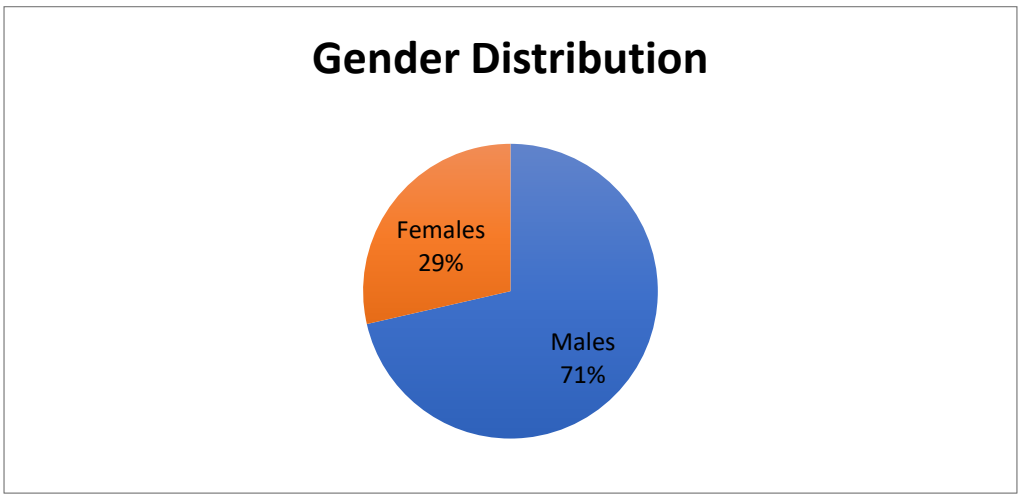


	0-10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years
Percentage	1.42%	0	1.42%	0	14.28%	40.00%	24.28%	15.71%	2.85%
Number of cases	1	0	1	0	10	28	17	11	2

Gender Distribution of patients [n=70]

Overall incidence of pancreatic lesion was higher in males constituting 71.42% [n=50] of all patients. Male to female ratio was 2.5:1.

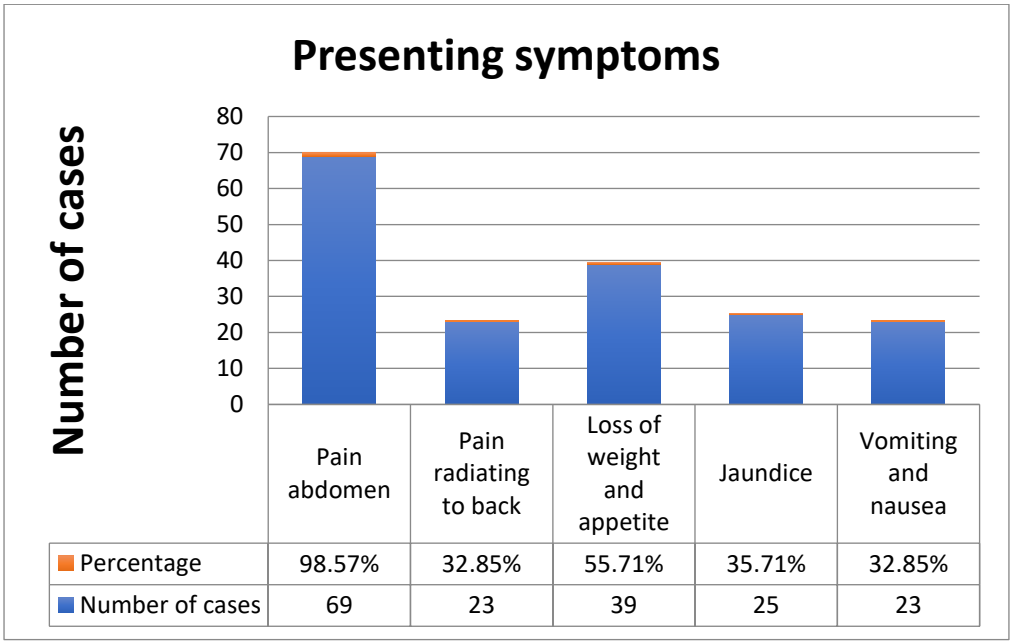
Figure 2- Gender distribution [n=70]



Clinical presentation of patients [n=70]

Pain abdomen was the most common symptom [n=69, 98.57%] followed by loss of weight and appetite [n=39, 55.71%]. Pain was radiating to back in 23 patients [32.85%] and jaundice was present in 25 patients [35.71%]. Most of the patients presented with more than one symptom, so there was overlap in categorizing patients on the basis of clinical signs and symptoms.

Figure 3- Clinical presentation [n=70]



Biochemical analysis and tumor marker levels [n=70]

Levels of serum calcium, amylase and lipase along with tumor markers like CA19-9 and CEA were done. 33 out of 70 patients had serum calcium levels done [47.14%] which were all within normal limits. Serum amylase level was done in 18 cases and were raised in 9 of them [50.00%] and serum lipase level was done in 20 cases, out of which 5 cases had raised levels [25.00%].

Tumor marker CA19-9 was done in 45 cases in the serum and was raised in 36 cases [80.00%]. Serum CEA level was raised in 20 cases out of 28 [71.42%].

Table 2 -Biochemical investigations and tumor markers [n=70]

Biochemical investigations and Tumor Markers	**Number of cases**	**Raised in**	**Percentage of cases with raised levels**
Serum Calcium	33	-	0.0%
Serum Amylase	18	9	50.00%
Serum Lipase	20	5	25.00%
CA19.9	45	36	80.00%
CEA	28	20	71.42%

Personal History

Out of 70 patients, 31 patients had history of chronic alcohol intake [44.28%]. 6 of the patients were both chronic alcoholic and smoker [8.5%].

Table 3- Personal history [n=37]

Personal History	Number of cases	Percentage
Alcohol	31	44.28%
Smoking with alcohol	6	8.5%

Spectrum of radiological lesions [n=53]

Out of 70 patients, 53 patients had record of radiological examination [n=53, 75.71%]. The commonest radiological finding was mass lesion likely malignant in 50 cases [94.33%]. 31 cases [58.49%] showed dilatation of the main pancreatic duct on imaging. 11 cases showed presence of stricturous areas in common bile duct. Accessory duct was dilated in 4 cases whereas 6 cases showed mass lesion causing obstructive biliopathy. 3 of the cases showed benign features [5.66%], out of which 2 cases were reported as Chronic pancreatitis and 1 was reported as Autoimmune pancreatitis. 51 cases were reported as solid lesion on imaging while 2 lesions were cystic in nature.

Table 4- Spectrum of radiological lesions [n=53]

Radiological findings	Number of patients	Percentage
Malignant	50	94.33%
Benign	3	5.66%

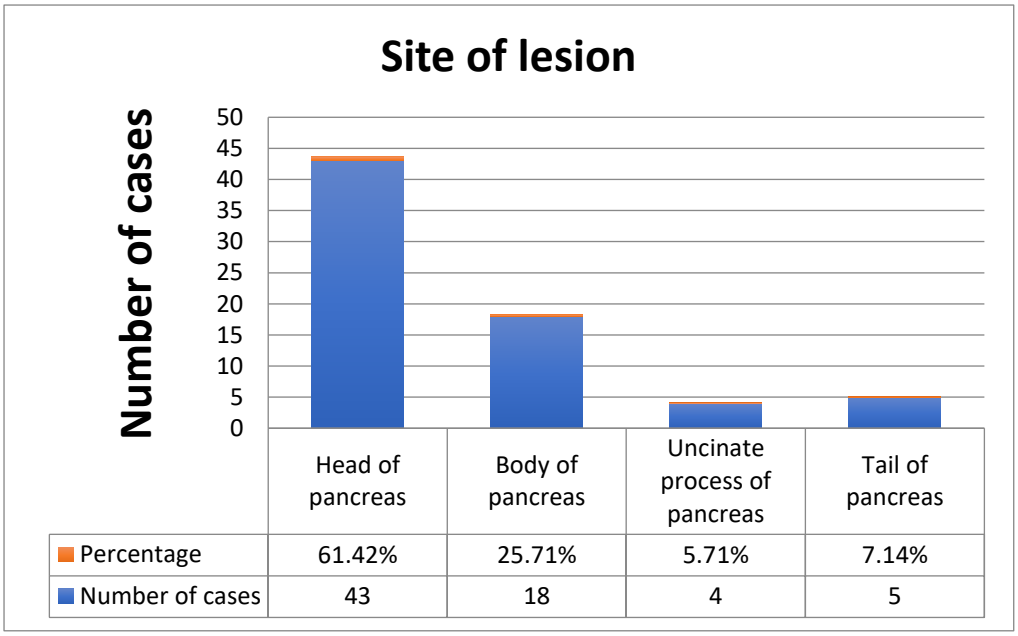
Site of Pancreatic lesion [n=70]

Majority of the patients had lesions in the head of the pancreas [n=43, 61.42%] followed by body of the pancreas [n=18, 25.71%]. Uncinate process was the least common site involved.

Table 5- Sites of pancreatic lesions [n=70]

Site of the lesion	Number of cases	Percentage
Head of pancreas	43	61.42%
Body of pancreas	18	25.71%
Uncinate process of pancreas	4	5.71%
Tail of pancreas	5	7.14%

Figure 4- Site of pancreatic lesions [n=70]



Mode of FNAC [n=70]

Majority of the patients underwent ultrasound guided FNAC procedure [n=54, 77.14%] followed by Endoscopic USG guided [n=16, 22.85%]. None of the patient underwent CT guided procedural technique.

Cytological categorization of pancreatic lesions

All the cases were categorized according to Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology into 6 broad categories that is Non diagnostic, Negative for malignancy, Atypical, Neoplastic (Benign or Others), Suspicious (for malignancy) and Positive or malignant.

Non diagnostic- This category included cases that were insufficient in cellularity (both quantitatively and/or qualitatively) to make a cytological diagnosis.

Negative for malignancy- This category included cases that lacked evidence of a malignant process. It comprised of benign pancreatic tissue, inflammatory lesions, pseudocyst and other cysts.

Atypical- This category contained spectrum of lesions which ranged from benign having minor degree of nuclear enlargement, hyperchromasia and anisonucleosis (atypia) to lesions showing features falling short of those fitting for definitive diagnosis of a carcinoma.

Neoplastic- This category was further divided into Benign and Others. Neoplastic;benign category includes the specimen with sufficient cellularity and representative of the area to be diagnostic of the benign neoplasm but without clinical, radiological or ancillary studies. Other category included neuroendocrine tumor, mucinous cystic neoplasm and solid pseudopapillary neoplasm.

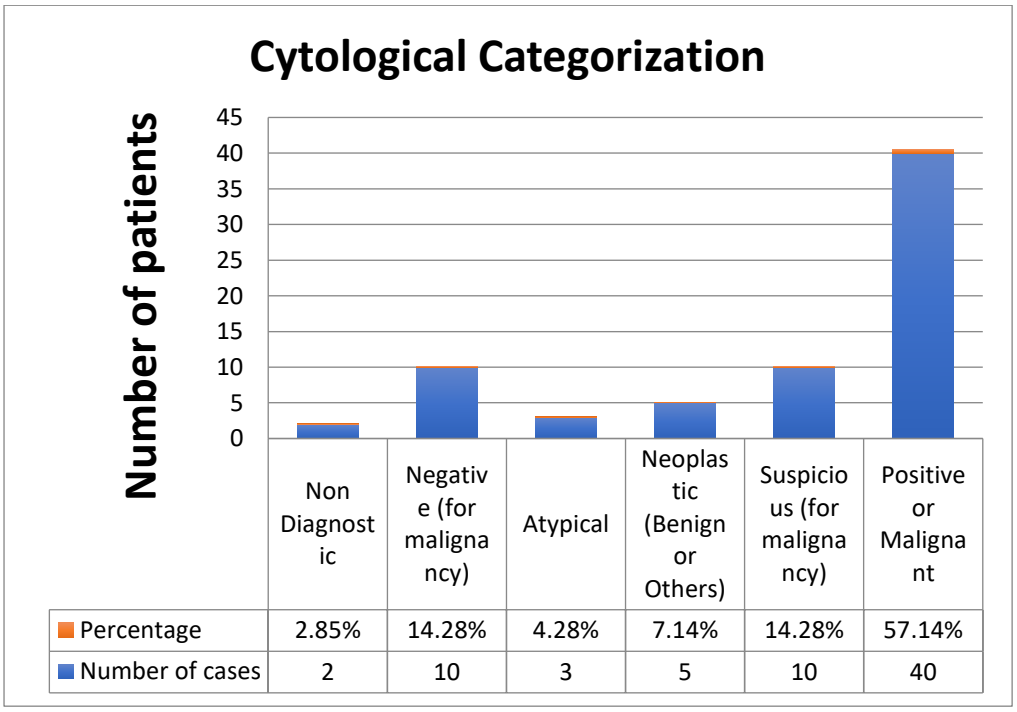
Suspicious (for malignancy)- This category had lesions that covered a range of atypias falling short of calling for a definitive diagnosis of malignancy. The main reason for failing to call Positive or Malignant was lack of ancillary testing or focal areas with features of definitive malignancy while others showing mild degree of nuclear atypia.

Positive or malignant- This category included lesions with cytological features definite for malignancy such as ductal adenocarcinoma of pancreas and its variants, Cholangiocarcinoma, Acinar cell carcinoma, Poorly differentiated (small or large cell) neuroendocrine carcinoma, Pancreatoblastoma, Lymphoma and Metastatic malignancy.

Table 6- Cytological categorization of pancreatic lesions [n=70]

Category	Number of cases	Percentage
Non Diagnostic	2	2.85%
Negative (for malignancy)	10	14.28%
Atypical	3	4.28%
Neoplastic (Benign or Others)	5	7.14%
Suspicious (for malignancy)	10	14.28%
Positive or Malignant	40	57.14%

Figure 5- Cytological categorization of pancreatic lesions [n=70]



40 out of 70 cases were grouped under positive or malignant category which comprised of 57.14% followed by suspicious (for malignancy) which were 14.28% [n=10]. 3 cases were reported as atypical [4.28%], while 5 cases[7.14%] were of neoplastic category among which all

were sub classified into others. 10 patients [14.28%] were categorized as negative (for malignancy) and only 2 samples [2.85%] were reported as non diagnostic.

Histo-pathological correlation was done in 50 cases [71.42%].

IHC studies were done in 18 cases [25.71%]

NON DIAGNOSTIC FOR EVALUATION [n=2]

In both the cases, there was presence of only fluid with thin extracellular mucin without any epithelial cells. Fluid biochemical analysis had not been performed hence these cases were reported as Non Diagnostic.

Age distribution for Non-Diagnostic category [n=2]

In this category, only 2 cases were reported which belonged to age group of 51-60 years[n=1, 50.0%] and 71-80 years [n=1, 50.0%].

Gender distribution of Non-Diagnostic category [n=2]

Both the patients were male [n=2, 100.0%].

Mode of FNAC in Non-Diagnostic category [n=2]

Both the cases of Non diagnostic category underwent Endoscopic USG guided FNAC [100.0%].

Site of Pancreatic lesion in Non-diagnostic category [n=2]

One of the patient had lesion in the head region of pancreas [50.0%], while other had lesion in the uncinate process of pancreas [50.0%].

Causes for Non-diagnostic category [n=2]

Out of 2 cases reported as non diagnostic, on imaging 1 case showed cystic lesion in uncinate process communicating with main pancreatic duct and accessory duct- likely mucinous cystic neoplasm which on cytology showed mainly hemorrhagic smears with scattered foamy macrophages (picture 1) with background showing thin extracellular mucin and no epithelial cells.

Other case showed features of carcinoma pancreas causing obstructive biliopathy with common hepatic artery encasement on imaging with cytological smears showing only thin scant mucin with occasional foamy macrophages. There was absence of epithelial cells for any comment in the smears examined (picture 2).

Correlation with Histopathology [n=2]

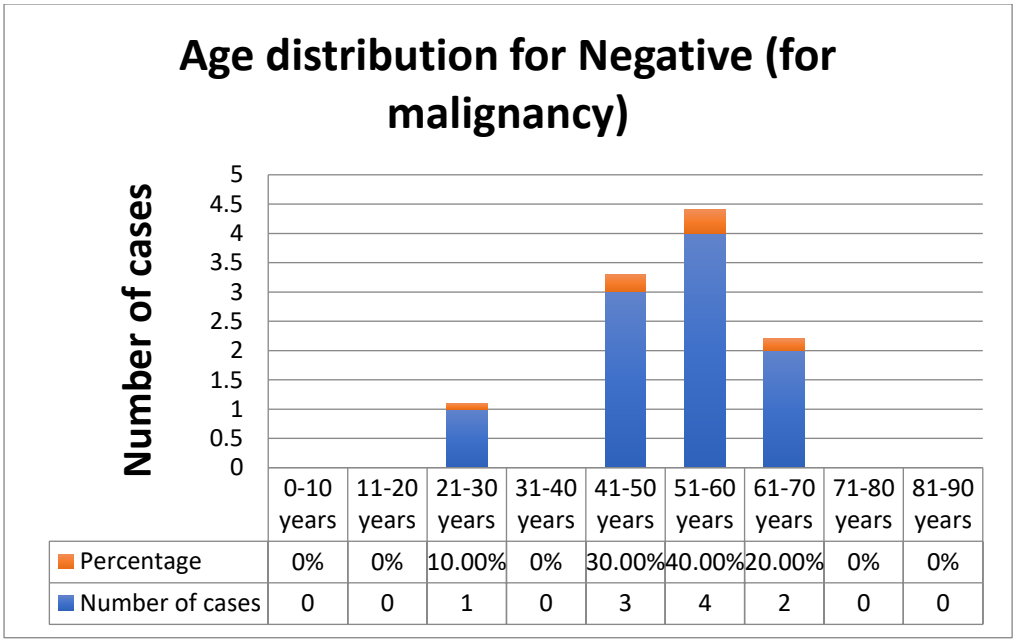
Histo-pathological correlation was available in one case only [50.0%], which was diagnosed as adenocarcinoma (picture 3 and 4). Final diagnosis of Ductal Adenocarcinoma was made after Immunohistochemical studies which showed that the tumor cells were immunopositive for CK7 and CEA and focal immunopositive for CK20.

NEGATIVE (FOR MALIGNANCY) [n=10]

Age distribution for Negative (for malignancy) [n=10]

Amongst negative (for malignancy) category, majority of the patients belonged to age group of 51-60 years [n=4, 40.0%]. Youngest patient was 25 years old and eldest was 65 years old with mean age of 50.5 years.

Figure 6- Age distribution for Negative (for malignancy) [n=10]



	0-10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years
Percentage	0%	0%	10.00%	0%	30.00%	40.00%	20.00%	0%	0%
Number of cases	0	0	1	0	3	4	2	0	0

Gender Distribution of Negative (for malignancy) [n=10]

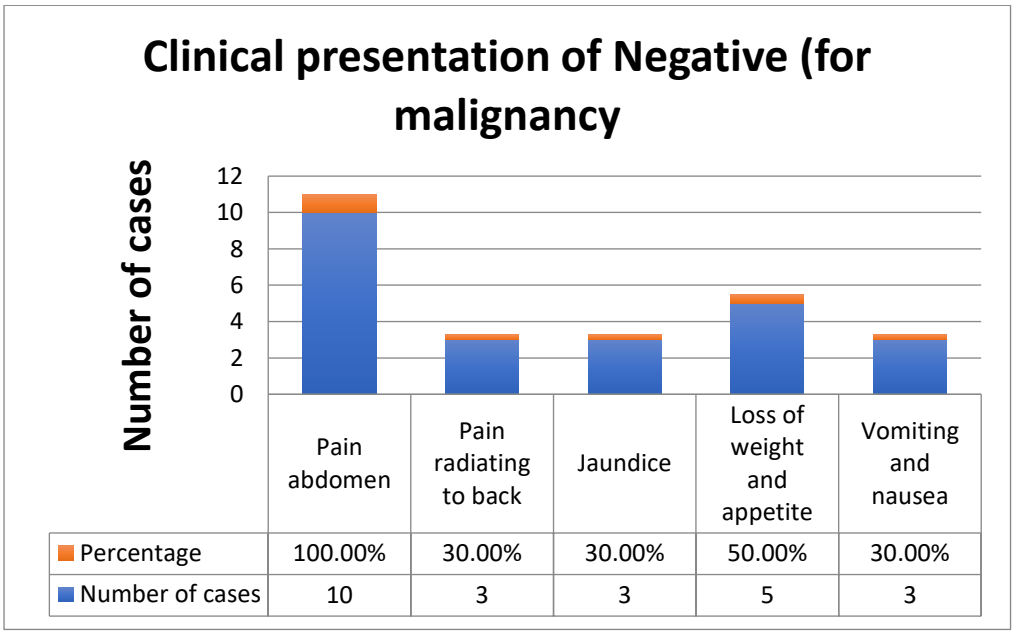
Majority of the patients reported as negative (for malignancy) were males [n=7, 70.0%] while 3 were females [30.0%]. Male to female ratio was 2.3:1.

Clinical presentation of patients with Negative (for malignancy) category [n=10]

All the patients reported as negative (for malignancy) presented with pain abdomen [n=10, 100.0%]. Out of 10, history of pain radiating to

back was present in 3 patients [30.0%]. 3 patients [30.0%] had history of jaundice and vomiting and nausea each. History of loss of weight and appetite was present in 5 patients [50.0%].

Figure 7- Clinical presentation of Negative (for malignancy) category [n=10].



Biochemical Investigations and Tumor markers

7 out of 10 cases of negative (for malignancy) category had serum biochemical investigations done. Serum calcium levels were within normal range in all the patients. Serum amylase and lipase levels were done in 3 cases [30.00%], out which serum amylase was raised in all 3 cases and serum lipase was raised in 2 cases only. However 1 case showed normal serum lipase levels.

CA19-9 levels were analyzed in 5 cases and were raised in only 3 cases [60.00%]. Out of these 3 cases 2 showed CA19-9 levels less than 100 U/ml while it was more than 100U/ml in the third case. CEA levels were also done in 5 cases and were raised in 2 cases but were less than 10ng/ml in both cases [40.00%].

Table 7- Biochemical Investigations and Tumor markers in Negative (for malignancy)

Biochemical Investigations and Tumor markers [n=10]	Number of patients	Raised in	Percentage
Serum Calcium	5	-	0.0%
Serum Amylase	3	3	100.00%
Serum Lipase	3	2	66.66%
CA19-9	5	3	60.00%
CEA	5	2	40.00%

Radiological findings in Negative (for malignancy) [n=6]

Radiological findings were available in 6 cases out of which 2 cases [20.00%] were reported as chronic pancreatitis and 1 case each was reported as autoimmune pancreatitis seen as mass lesion in head region, chronic calcified pancreatitis, cystic lesion of pancreas and pancreatic neoplasm.

Mode of FNAC in Negative (for malignancy) [n=10]

Majority of the patients underwent endoscopic ultrasound guided FNAC [n=7, 70.0%], while 3 patients had undergone ultrasound guided FNAC [30.0%].

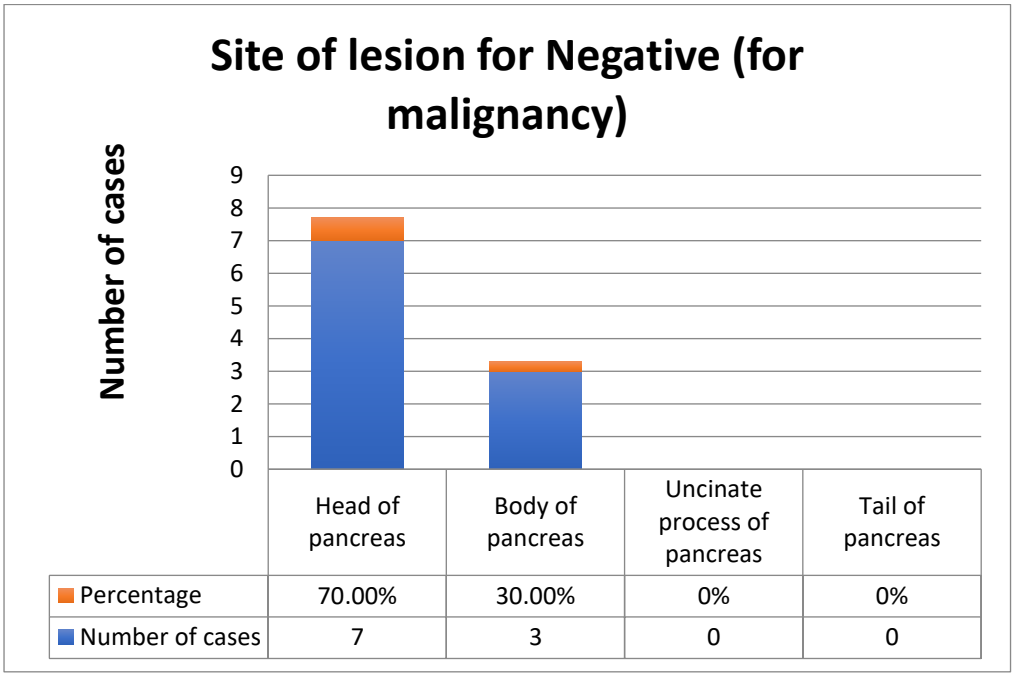
Table 8- Mode of FNAC in Negative (for malignancy) [n=10]

Mode of FNAC	Number of patients	Percentage
Endoscopic Ultrasound guided	7	70.0%
Ultrasound Guided	3	30.0%

Site of pancreatic lesions in Negative (for malignancy) category [n=10]

Majority of the patients had lesion in head region of the pancreas [n=7, 70.0%], while 3 patients out of 10 had lesion in body of pancreas [30.0%].

Figure 8- Site of lesion for Negative (for malignancy) [n=10]



Diagnostic spectrum for lesion of Negative (for malignancy) category [n=10]

Among 10 cases, 1 case showed necrotic debris, crystals, foamy macrophages with scattered inflammatory cells mainly histiocytes along with yellow pigment and lymphocytes. Occasional hemosiderin laden macrophages were also noted and was reported as pseudocyst (picture 5). No radiological investigations were found in this case.

Aspirate from another case showed presence of few clusters of benign ductal epithelial cells against a fluidy background along with foamy macrophages and debris and was diagnosed as benign cystic lesion (picture 6). No cyst fluid biochemical analysis was available. Radiological investigation in this case was suggestive of cystic lesion in the superior aspect of head of pancreas.

2 cases showed collections of epithelioid cells forming granulomas with scattered histiocytes, lymphocytes and multinucleated giant cells against a background of necrosis and were reported as granulomatous pancreatitis (picture 7). 20%ZN for AFB was applied in both the cases and it was non contributory in both of them. On follow up these 2 cases, it was found that one of the patient had undergone anti-

tubercular treatment for period of 6 months. Cell block was made of the aspirate material which was inadequate due to scant cellularity. The other patient with granulomatous pancreatitis was lost for further follow up.

6 cases were reported as Negative for malignancy-not otherwise specified. These cases showed pancreatic acinar cells with clusters of benign pancreatic ductal epithelial cells few of which were displaying no significant atypia (picture 8 and 9). Histo-pathological evaluation was done in one case which was suggestive of fat necrosis (picture 10).

Table 9- Diagnostic spectrum for lesions of Negative (for malignancy) category[n=10].

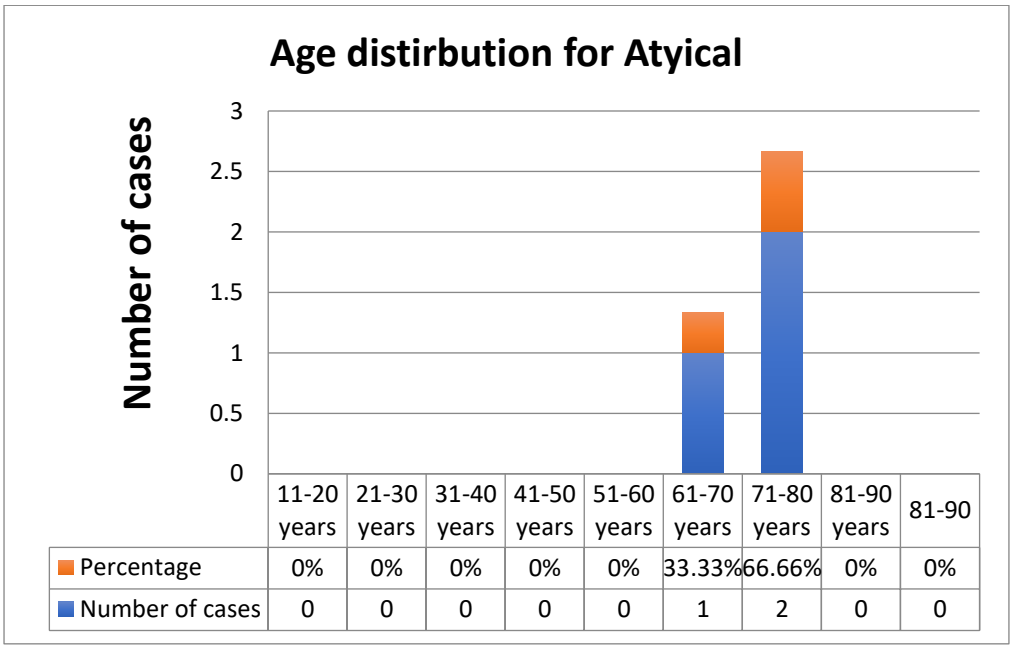
Cytological diagnosis	Cytological features	Special stains [n=2]	Radiological findings [n=6]	Histology/Cell blocks [n=2]	Percentage
Granulomatous inflammation [n=2]	Well formed epithelioid cells granulomas with necrosis [n=2]	20%ZN-non contributory [n=2]	MRI abdomen-Exophytic mass arising from body of pancreas	-	20.00%
			Not done	Cell block-Inadequate for opinion [n=1]	
Pseudocyst [n=1]	Foamy macrophages and necrotic debris. Crystals and inflammatory cells were also noted.	-	Not done	-	10.00%
Benign cystic lesion [n=1]	Fluid rich background along with foamy macrophages. Clusters of benign pancreatic epithelial cells	-	CECT abdomen-Cystic lesion in superior aspect of head of pancreas.	-	10.00%
Negative for malignancy, NOS [n=6]	Sheets of benign pancreatic epithelial cells and acinar cells.	-	Autoimmune pancreatitis [n-1]	Fat necrosis [n=1]	60.00%
			Chronic pancreatitis [n=2]	-	
			Chronic Calcified Pancreatitis [n=1]	-	
			Not done[n=2]	-	

ATYPICAL

Age distribution for Atypical [n=3]

In Atypical category, 2 cases belonged to age group of 61-70 years [66.66%] and 1 case was from 51-60 years of age group [33.33%].

Figure 9- Age distribution for Atypical [n=3]



Gender distribution for Atypical [n=3]

Among the 3 patients, 2 were male [66.66%] and 1 was female [33.33%] with male to female ratio of 2:1.

Clinical presentation of Atypical category [n=3]

All the 3 patients presented with Pain abdomen [100.0%], out of which 1 had history of pain radiating to back [33.33%]. Loss of weight and appetite was seen in all the 3 cases[100.0%] with presence of jaundice in 1 patient only [33.33%]. 2 patients [66.66%] also had complaint of vomiting and nausea [66.66%].

Table 10- Clinical presentation of Atypical [n=3]

Clinical presentation	Number of cases	Percentage
Pain abdomen	3	100.0%
Loss of weight and appetite	3	100.0%
Vomiting and nausea	2	66.66%
Pain radiating to back	1	33.33%
Jaundice	1	33.33%

Radiological findings in Atypical Category [n=3]

Radiological investigations were done in all the 3 cases, out of which one showed poorly marginated mass in the body of pancreas causing marked dilatation of main pancreatic duct-likely malignant. Another case was reported as Neuroendocrine tumor which showed large solid heterogenous mass in distal body and pancreatic tail with extension and third case was reported as mass lesion of unknown etiology causing significant luminal narrowing.

Biochemical Investigations and Tumor markers

Out of 3 cases, serum calcium along with serum amylase and lipase levels were done in 2 cases and within normal limits. CA19-9 levels were done in 3 cases and were raised in all while CEA level was done 1 case and was raised. CA19-9 was more than 100U/ml in all the cases. CEA level was also more than 2 times the upper limit.

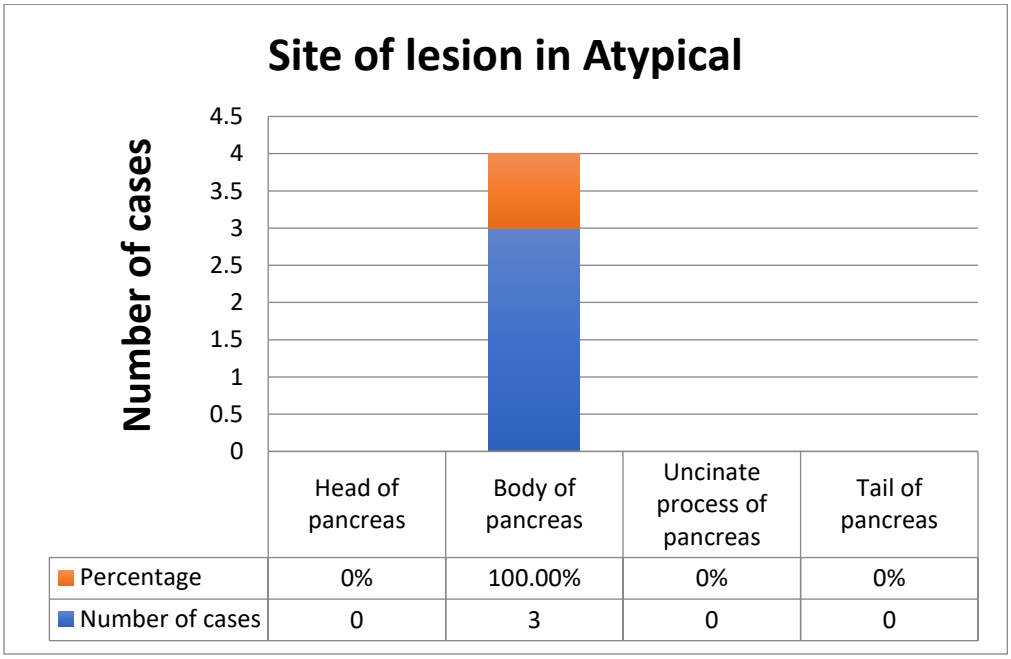
Mode of FNAC in Atypical [n=3]

Out of 3 patients, 2 patients underwent ultrasound guided FNA [66.66%] and 1 patient underwent endoscopic USG guided procedure [33.33%].

Site of pancreatic lesions in Atypical [n=3]

In Atypical category, FNAC was done from body of pancreas in all the 3 cases [100.0%].

Figure 10- Site of lesion in Atypical [n=3]



Diagnostic spectrum of lesions in Atypical category [n=3]

All the cases reported as Atypical on cytology were solid in nature, the smears were cellular in all the three cases [100.00%] and the cells were arranged in cohesive clusters, two cases [66.66%] showed papillaroid clusters and 1 case [33.33%] showed monolayered sheet as well with singly scattered cell population.

All the cases exhibited mild degree of anisonucleosis [2:1] with altered N:C ratio, nuclear crowding and overlapping with focal irregularity of nuclear contours. The nucleoli were inconspicuous in two cases and conspicuous in one case with moderate cytoplasm in all cases. The background was mucinous in all the three cases [100.00%] with two cases also showing inflammatory infiltrates both acute and chronic in the background [66.66%]. On analyzing these three cases, the nuclear changes were focal and incomplete. None of the cases displayed significant anisonucleosis, macronucleoli or background necrosis to call it malignant. True nuclear moulding was also not seen in these smears, hence precluding a malignant interpretation (picture 11,12 and 13).

Architectural and cytological aberrations seen as nuclear enlargement with focal crowding of the nuclei along with slight nuclear membrane irregularities, insignificant anisonucleosis with a clean background

devoid of necrosis were morphological features which did not reach the degree necessary to be considered malignant. However, there were more than those expected to seen as reactive atypia. .

Trucut biopsies for histopathological evaluation were done in 2 cases. Both the cases were diagnosed as Adenocarcinoma with background showing mucin on histology. Immunohistochemical study was performed in 1 case, which was in concordance with histopathology. Tumor cells were immunopositive for CDX2, CK7 (diffuse strong positive), immunonegative for CK20, Chromogranin and Synaptophysin. MiB1 was 70% in highest proliferating areas. The reason for discordance with histological diagnosis was attributed to sampling error.

Table 11- Diagnostic spectrum of lesions in Atypical category [n=3]

Cytological diagnosis	**Cytological features**			**Radiological findings [n=3]**	**Histological diagnosis/ IHC [n=2]**
Atypical-Category III [n=3]	Architecture	Cohesive clusters	3	Likely Non Functional Neuroendocrine Tumor [n=1]	Ductal Adenocarcinoma
		Papillaroid clusters	2		
		Monolayered sheet	1		
	Cytology	High N:C	3		
		Anisonucleosis	2:1 in all cases		
		Prominent nucleoli	Absent	Malignant process [n=1]	Ductal Adenocarcinoma
		Irregular nuclear contours	3		
	Background	Necrosis	Absent	Mass lesion of unknown etiology [n=1]	-
		Mucin	3		

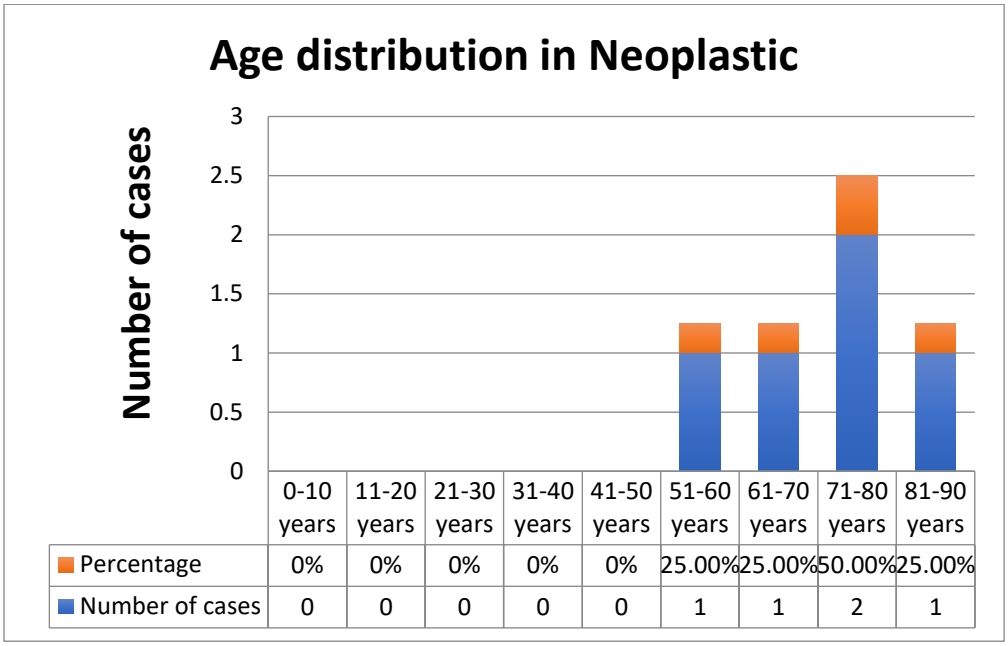
NEOPLASTIC

Neoplastic category was further divided into 2 subgroups- Benign and Others. All the cases fell in the category of Others.

Age distribution in Neoplastic [n=5]

2 cases out of 5 belonged to 71-80 years of age group while rest of the 3 cases were from 51-60, 61-70 and 81-90 years of age group each.

Figure 11- Age distribution in Neoplastic [n=5]



Gender distribution in Neoplastic [n=5]

Out of 5 patients diagnosed as Neoplastic- Category IV, 4 were males [75.0%] and 1 was female [25.0%]. Male to female ratio was 4:1.

Clinical presentation of patients in Neoplastic category [n=5]

Among the 5 patients, 4 patients [80.00%] presented with pain abdomen. 2 patients complained of pain radiating to back [40.00%]. Loss of weight and appetite along with jaundice was seen in 2 of the patients [40.00%]. None of the patient had any history of vomiting and diarrhea.

Table 12- Clinical presentation of patients in Neoplastic category [n=5]

Clinical presentation	Number of cases	Percentage
Pain abdomen	4	80.00%
Pain radiating to back	2	40.00%
Loss of weight and appetite	2	40.00%
Jaundice	2	40.00%
Vomiting and nausea	0	0%

Biochemical investigations and Tumor markers

Serum calcium levels were available in 2 cases and were in normal limits, however serum amylase and lipase levels were only investigated in 1 case and were raised. CA19-9 was raised in 2 cases out of 3 and CEA level was done in 1 case and was within normal limits.

Table 13- Biochemical investigations and Tumor markers in Neoplastic

Biochemical investigations and Tumor markers	Number of cases	Raised in	Percentage
Serum Calcium	2	-	0.0%
Serum Amylase	1	1	100.00%
Serum Lipase	1	1	100.00%
CA19-9	3	2	66.66%
CEA	1	-	0.0%

Radiological Findings in Neoplastic [n=4]

4 out of 5 patients underwent radiological investigation. 2 of the cases were reported as pancreatic malignancy on CECT while 1 case was reported as hypoechoic lesion -? etiology on Ultrasonography. 1 case showed the features of pancreatitis on CT abdomen.

Mode of FNAC in Neoplastic [n=5]

Out of 5 patients reported as Neoplastic- Category IV, in 4 patients [80.00%], mode of FNAC was Ultrasound Guided and 1 patient [20.00%] underwent Endoscopic USG guided procedure.

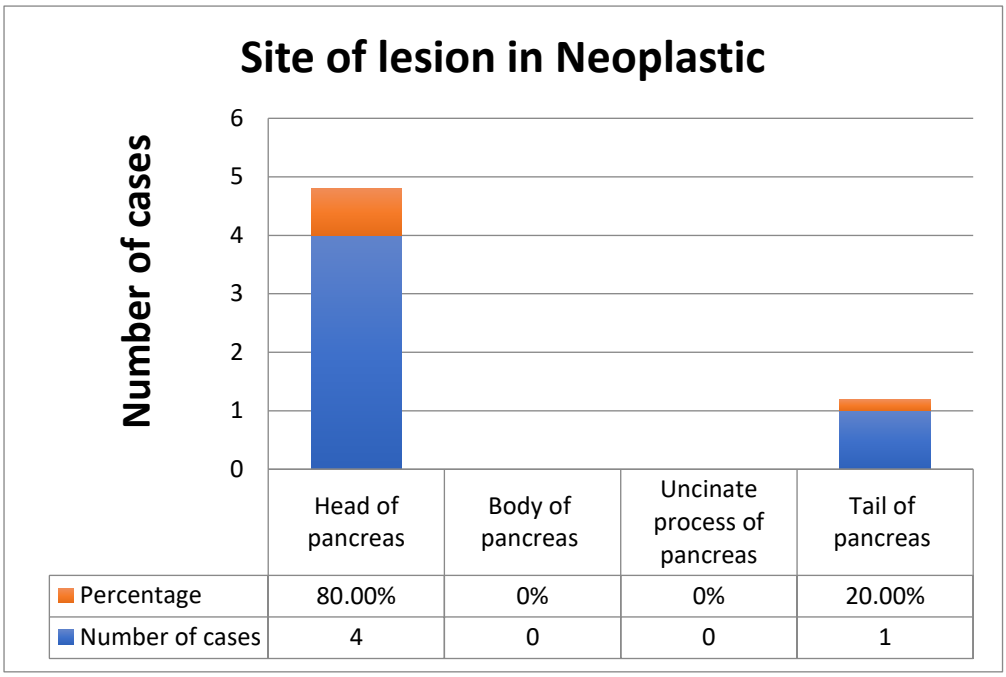
Table 14- Mode of FNAC in Neoplastic[n=5]

Mode of FNAC in Neoplastic	Number of cases	Percentage
Ultrasound Guided	4	80.00%
Endoscopic USG guided	1	20.00%

Site of lesion in Neoplastic [n=5]

4 out of 5 patients [n=4, 80.00%] reported as Neoplastic had lesions in the head region of pancreas. 1 patient had lesion in tail of pancreas.

Figure 12- Site of lesion in Neoplastic [n=4]



Diagnostic spectrum of lesions diagnosed as Neoplastic [n=5]

Out of the 5 cases reported as Neoplastic-Category IV, all were subcategorized into others. All the cases were cellular [100.00%] with 2 cases diagnosed as Mucinous cystic neoplasm. The radiological evaluation was done in only one case reported as Mucinous neoplasm which showed ill defined hypo-enhancing mass lesion involving head and uncinate process with double duct sign and obstructive biliopathy with encasement of superior mesenteric artery- Advanced pancreatic malignancy. Fine needle aspiration yielded thick colloid like extracellular mucin in both the cases. Cytological evaluation of both the cases revealed extracellular mucin amidst which was present low-grade mucinous epithelium exhibiting low-grade dysplasia having scant cellularity. Smears also showed single cells along with flat sheets of bland glandular epithelial cells with round and regular nuclei, evenly clumped chromatin and inconspicuous nucleoli. The nuclei were basally located with apical cytoplasm showing mucin with presence of

foamy histiocytes. There was no significant nuclear atypia, mitosis or presence of drunken honeycomb appearance on cytology to call it a malignant aspirate (picture 14 and 15). Histological examination of one of these cases showed presence of tumor cells arranged in glandular configuration having moderate pleomorphic vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm with mucinous background and was reported as Adenocarcinoma. However, no histological examination was available for the other case.

1 case was reported as Solid pseudo papillary neoplasm, which showed cellular smears composed of uniform cells in cohesive clusters often branching with papillary configuration having thin fibrovascular core. Individual tumor cells were uniform in size with oval to bean shaped nucleus with mild degree of anisonucleosis, fine granular chromatin with inconspicuous nucleoli. Background showed presence of hemorrhagic debris along with histiocytes and multinucleated giant cells. No mitotic activity was noted. Some of the cells also showed perinuclear vacuolization. Based on presence of fibrovascular core and nuclear grooving and granular chromatin, it was reported as solid pseudopapillary neoplasm (picture 16 and 17). Pancreatectomy specimen was received of this patient and histopathological examination was done which showed tumor cells having monomorphic appearance with stippled chromatin-suggestive of neuroendocrine tumor (picture 18). IHC showed immunopositivity for CDX-2, synaptophysin, dot positivity for chromogranin and negative nuclear staining for beta catenin. Mib1 was 1% in highest proliferating areas. This led to diagnosis of neuroendocrine tumor on histology (picture 19 and 20). Solid pseudopapillary neoplasm is a close differential of neuroendocrine tumor.

2 cases showed cellular smears having singly scattered and tiny dyscohesive clusters giving it a ‘solid cellular smear pattern’ or rosettes of monomorphic cells with regular round bland nucleus, stippled and evenly distributed chromatin, inconspicuous nucleoli with scant amount of cytoplasm. Few of the cells also showed dense and eccentric nuclei giving it a plasmacytoid appearance. There was no necrosis or mitosis

in the smears examined. These were reported as Pancreatic neuroendocrine tumor (picture 21 and 22). Histological examination of one of these cases showed feature of chronic pancreatitis while there was no biopsy available in other case.

None of the case was reported as Neoplastic:Benign in this category on cytology.

Table 15- Diagnostic spectrum of lesions in Neoplastic category-other [n=5]

Cytological diagnosis	**Cytological features**	**Radiological findings [n=4]**	**Histopathology/ Cell block [n=3]**
Mucinous cystic neoplasm [n=2]	Cohesive clusters and irregular clusters of atypical epithelial cells displaying nuclear enlargement with focal nuclear crowding and overlapping. The background was mucinous.	Advanced pancreatic malignancy [n=1]	Adenocarcinoma (with mucinous background) [n=1]
		-	-
Pancreatic Solid Pseudo-papillary neoplasm [n=1]	Papillaroid clusters and singly scattered uniform to mildly pleomorphic cells with presence of foamy macrophages and multinucleated giant cells. Nuclear grooving and indentation. Thin fibrovascular septations seen.	Pancreatic Adenocarcinoma [n=1]	Neuroendocrine tumor of pancreas [n=1]
Pancreatic neuroendocrine tumor [n=2]	Moderately cellular smears with presence of monotonous population of small to medium sized polygonal epithelial cells with salt and pepper chromatin.	Hypoechoic lesion in pancreatic head [n=1]	Chronic Pancreatitis [n=1]
		Mass lesion-likely secondary to Chronic pancreatitis [n=1]	-

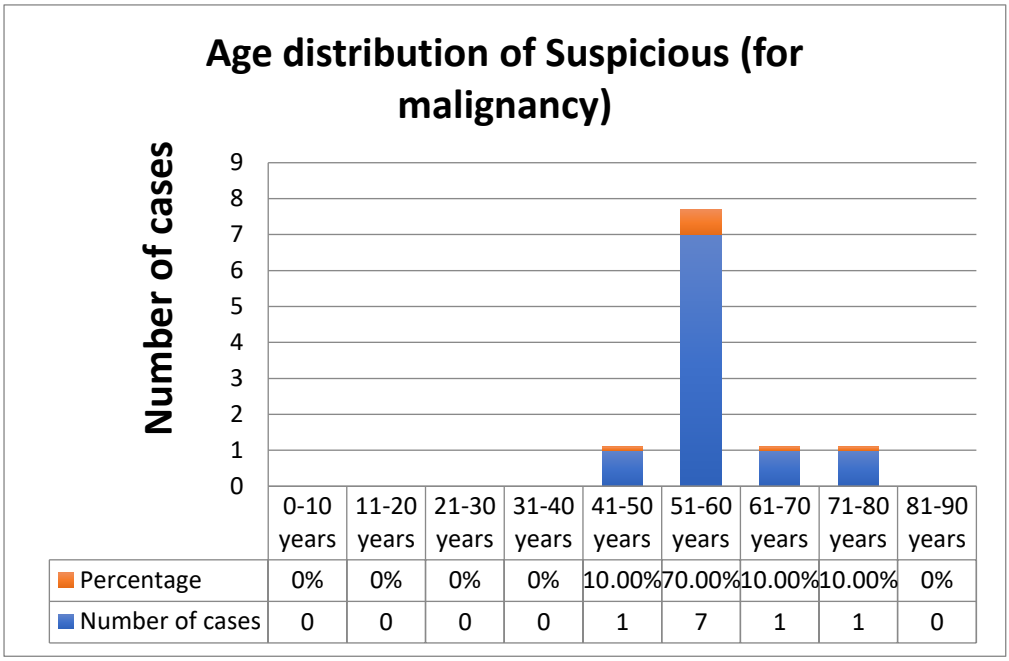
SUSPICIOUS (FOR MALIGNANCY)

Out of the 70 FNAC cases of pancreas reported in our study, 10 were reported as Suspicious (for malignancy) [14.28%].

Age distribution of Suspicious (for malignancy)[n=10]

All patients belonged to the age group of more than 40 years with majority of the cases [n=7, 70.0%] belonging to age group of 51-60 years. 1 case each belongs to age group of 41-50, 61-70 and 71-80 years [10.0% each].

Figure 13- Age distribution of Suspicious (for malignancy) [n=10]



	0-10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years
Percentage	0%	0%	0%	0%	10.00%	70.00%	10.00%	10.00%	0%
Number of cases	0	0	0	0	1	7	1	1	0

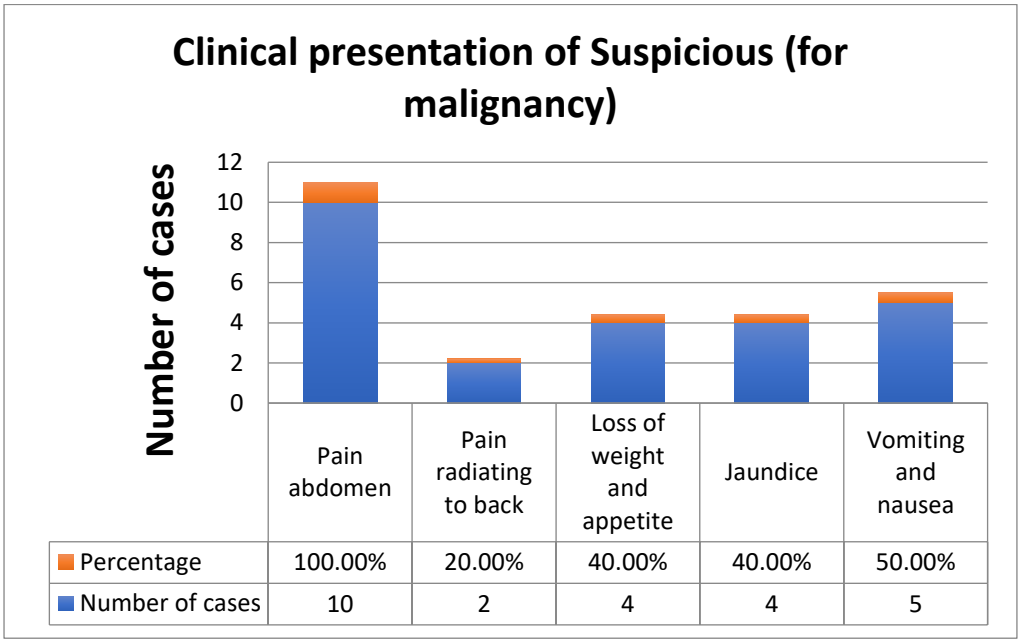
Gender distribution of Suspicious (for malignancy)[n=10]

8 cases in this category were males [80.0%] and 2 were females [20.0%]. Male to female ratio was 4:1.

Clinical presentation of patients in Suspicious (for malignancy) category [n=10]

All the patients in this category presented with pain abdomen [100.0%], in which 2 of the patients had complaint of pain radiating to back [20.0%]. 4 patients had history of loss of weight and appetite [40.0%]. 4 patients had jaundice of presentation [40.0%] and 5 patients had complaint of vomiting and nausea [50.0%].

Figure 14- Clinical presentation in Suspicious (for malignancy) category [n=10]



Biochemical Investigations and Tumor markers [n=7]

7 out of 10 patients underwent biochemical investigations and had normal serum calcium levels. Serum amylase levels were investigated in 4 cases and were raised in only 2 cases while serum lipase was investigated in 6 cases and was raised in 3 of them. CA19-9 levels were raised in 4 out of 6 cases being analyzed and CEA was raised in all the 5 cases in which CEA levels were recommended.

Table 16- Biochemical Investigations and Tumor markers in Suspicious (for malignancy)

Biochemical Investigations and Tumor markers	Number of cases	Raised in	Percentage
Serum Calcium	7	-	0.0%
Serum Amylase	4	2	50.00%
Serum Lipase	6	3	50.00%
CA19-9	6	4	66.66%
CEA	5	5	100.00%

Radiological Findings in Suspicious (for malignancy) [n=8]

8 out of 10 patients underwent radiological studies in form of CT or USG and were reported as malignant in 7 cases [70.00%] with dilation of main pancreatic duct and obstructive biliopathy. However one case showed features of autoimmune pancreatitis on imaging.

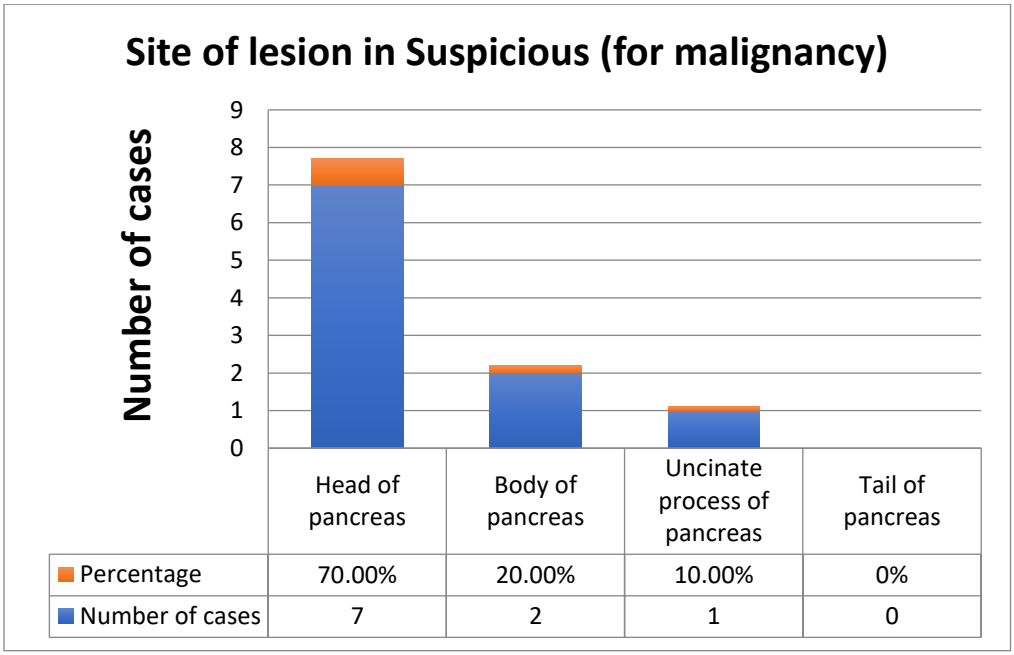
Mode of FNAC in Suspicious (for malignancy)

8 of these patients underwent ultrasound guided FNAC procedure [80.0%] and only 2 patients underwent endoscopic USG guided FNAC [20.0%].

Site of lesion in Suspicious (for malignancy) [n=10]

Majority of the patients diagnosed as suspicious (for malignancy) had lesion in the head region of pancreas [n=7, 70.0%]. Lesion in body of pancreas was seen in 2 patients [20.0%] and 1 patient had lesion in uncinate process of the pancreas [10.0%].

Figure 15- Site of lesion in Suspicious (for malignancy) [n=10]



Diagnostic spectrum of lesions in Suspicious (for malignancy) category [n=10]

Suspicious smear means there is significant alteration in the architectural and individual cell morphology but not all the criteria are met to call it as Positive or Malignant. Cases reported as suspicious (for malignancy) showed cellular smears in 9 of the cases [90.00%]

with one case showing scant cellularity [10.00%]. 1 case with scant cellularity was reported as Suspicious showed some features pointing towards malignancy which were significant anisonucleosis (4:1), nuclear enlargement, overlapping and crowding and presence of necro-inflammatory background, however it lacked macronucleoli & had a compromised cellularity leading to a Suspicious categorization. On analyzing the morphological features, there was marked anisonucleosis [4:1] in 4 cases [40.00%] but due to absence of prominent nucleoli and necrotic background; the diagnosis of malignancy was not made. Moderate anisonucleosis [3:1] was seen in 5 cases [50.00%] and 1 case showed mild degree of anisonucleosis [2:1]. The nucleoli were inconspicuous in 7 cases [70.00%] with conspicuous nucleoli in 30.00% cases [n=3]. These features were not present in all the groups and clusters of cells.

Though nuclear enlargement, nuclear crowding/ overlapping, variable anisonucleosis was present in all the cases examined; lack of macronucleoli and tumor diathesis led these cases being reported as Suspicious (picture 23).

Of all the cases reported as Suspicious (for malignancy), trucut biopsy was taken in 8 cases [80.0%]. Histo-pathological examination in these 8 cases were done and 7 cases were reported as adenocarcinoma [70.0%], while 1 case was reported as Non diagnostic due to insufficient cellularity. Immunohistochemical studies were done in 2 cases of trucut biopsies and were finally diagnosed as Ductal Adenocarcinoma. The cases reported as Suspicious were lacking few of the features definitive for malignancy but on histology, there was glandular configuration of tumor cells exhibiting nuclear pleomorphism having vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm.

Table 17- Diagnostic spectrum of lesions in Suspicious (for malignancy) category [n=10].

Cytological diagnosis	**Cytological features**			**Radiological findings [n=8]**	**Histological diagnosis [n=8]**
Suspicious of malignancy [n=10]	Architecture	3D clusters	3	Mass lesion-likely primary. [n=5]	Ductal adenocarcinoma [n=7]
		Cohesive clusters	9		
		Singly scattered	8		
		Papillaroid clusters	2		
		Drunken honeycomb	4		
	Anisonucleosis	4:1	4		
		3:1	5		
		2:1	1		
		Nuclear crowding and overlapping	10		
	Background	Mucin	3	Autoimmune pancreatitis. [n=1]	Inadequate for opinion-Non Diagnostic [n=1]
		Necrosis	2		
				Mass lesion-likely neoplastic [n=2]	-

POSITIVE OR MALIGNANT

Out of 70 cases in our study, 40 were diagnosed as Positive or Malignant [57.14%]. Out of these 40 cytologically positive or malignant cases, 37 [52.85%] were diagnosed Adenocarcinoma , while 2 cases [2.85%] were reported as Malignant aspirate- Adenocarcinoma with mucinous differentiation. 1 patient was diagnosed as Malignant round cell tumor-possibly Lymphoma.

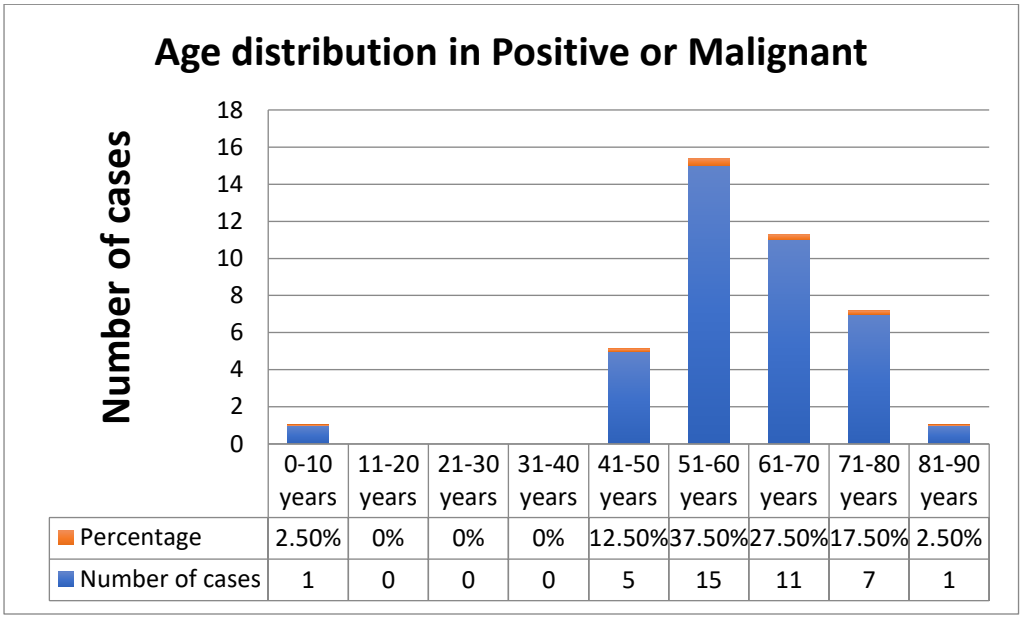
Age distribution of Positive or Malignant [n=40]

Out of 40 patients, majority of patients [n=15,42.25%] belonged to age group of 51-60 years. Youngest patient was 10 years old who was diagnosed as lymphoma and eldest was 88 years old with mean age of 61 years.

Table 18- Age distribution of Positive or Malignant [n=40]

Age distribution	Number of cases	Percentage
0-10 years	1	2.50%
11-20 years	0	0%
21-30 years	0	0%
31-40 years	0	0%
41-50 years	5	12.50%
51-60 years	15	37.50%
61-70 years	11	27.50%
71-80 years	7	17.50%
81-90 years	1	2.50%

Figure 16- Age distribution in Positive or Malignant [n=40]



	0-10 years	11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	61-70 years	71-80 years	81-90 years
Percentage	2.50%	0%	0%	0%	12.50%	37.50%	27.50%	17.50%	2.50%
Number of cases	1	0	0	0	5	15	11	7	1

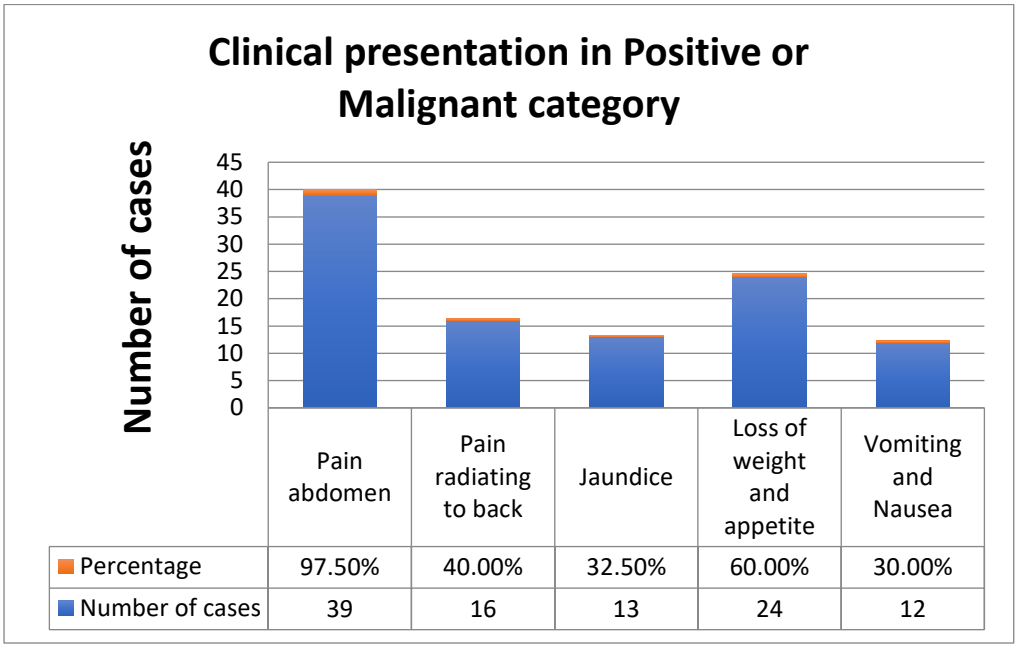
Gender distribution in Positive or Malignant [n=40]

Out of 40 patients, majority affected were males [n=27, 67.50%], while 13 females were diagnosed as positive in our study [32.50%]. Male to female ratio was 2.1:1.

Clinical presentation of patients in Positive or Malignant category [n=40]

Majority of patients presented with pain abdomen [n=39, 97.50%], out of which 16 patients had complaint of pain radiating to back [40.00%]. 13 patients had jaundice [32.50%]. Loss of weight and appetite was reported by 24 patients [60.00%] while history of vomiting and nausea was present in 12 patients [30.00%].

Figure 17- Clinical presentation in Positive or Malignant category [n=40]



Biochemical investigations and Tumor markers

Serum Calcium levels were done in 16 cases and were within normal range. Serum amylase and lipase levels were analyzed in 8 patients amongst which 2 cases showed raised serum amylase levels while lipase was normal in all the 8 cases. CA19-9 levels were raised in 24 cases out of 28 [85.71%] and CEA levels were raised in 12 out 15 cases [80.00%]

Table 19- Biochemical investigations and Tumor markers in Positive or Malignant

Biochemical investigations and Tumor markers	Number of patients	Raised in	Percentage
S.Calcium	16	-	0.0%
S.Amylase	8	2	25.00%
S.Lipase	8	-	0.0%
CA19-9	28	24	85.71%
CEA	15	12	80.00%

Radiological Findings in Positive or Malignant [n=30]

Various imaging modalities were used while diagnosing pancreatic lesions on imaging for example MRCP, CECT, USG and PET CT. 30 out of 40 patients underwent radiological investigations. 29 out 30 cases [96.66%] showed features of malignancy on radiography showing dilation of main pancreatic duct with obstructive biliopathy and mass lesions in different regions of pancreas while 1 case was reported as peripancreatic fat inflammation and collection- favouring lymphoma on imaging.

Mode of FNAC in Positive or Malignant [n=40]

Majority of patients diagnosed as Positive or Malignant underwent Ultrasound Guided FNAC procedure [n=37, 92.50%] while 3 patients underwent Endoscopic USG guided FNAC procedure [7.50%].

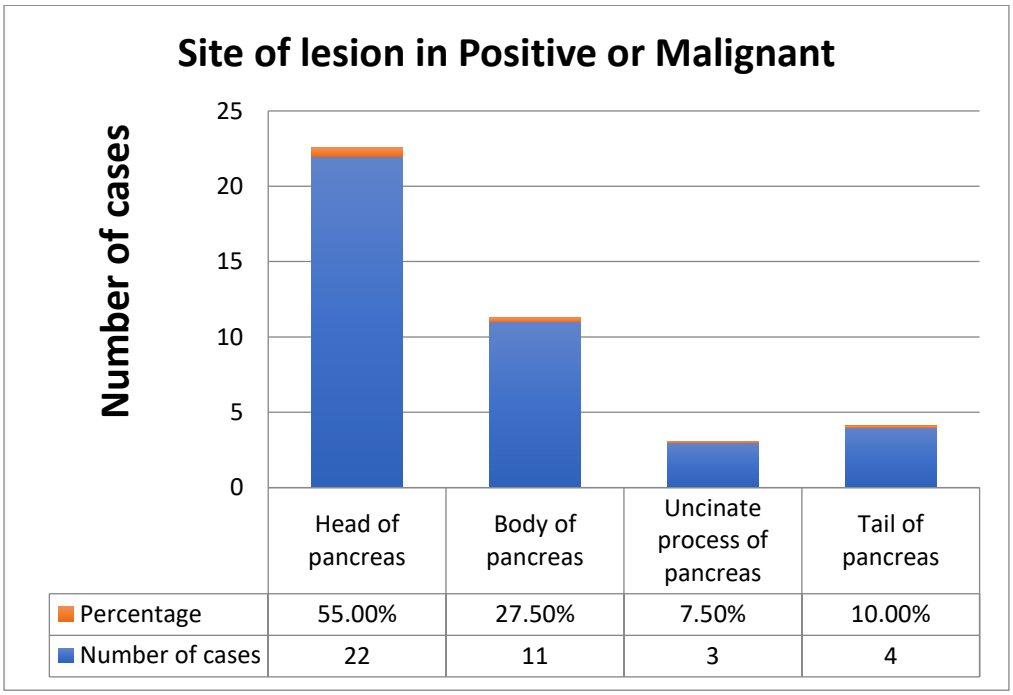
Table 20- Mode of FNAC in Positive or Malignant [n=40]

Mode of FNAC	Number of cases	Percentage
Ultrasound guided	37	92.50%
Endoscopic USG guided	3	7.50%

Site of lesion in Positive or Malignant [n=40]

Majority of the patients presented with lesion in the head region of the pancreas [n=22, 55.0%] followed by body of pancreas [n=11, 27.50%]. Uncinate process was involved in 3 patients [7.50%] and tail of pancreas was involved in 4 cases [10.00%].

Figure 18- Site of lesion in Positive or Malignant category [n=40]



Diagnostic spectrum of lesions in Positive or Malignant category [n=40]

Out of 40 cases, 39 were reported as ductal adenocarcinoma. Smears were highly cellular in 12.50% cases [n=5] and 87.50% [n=35] were cellular. Smears showed three-dimensional clusters in 25.00% cases [n=10], papillaroid clusters in 7.50% [n=3], drunken honeycomb appearance in 18 cases [45.00%], cohesive clusters and singly scattered large atypical cell population as well in 97.50% [n=39] cases. There was significant anisonucleosis in 31 cases [77.50%] and moderate anisonucleosis in 8 cases [20.00%]. The cases, which showed moderate anisonucleosis, also showed other features that were consistent with malignancy. There was presence of drunken honeycomb pattern (picture 24) with prominent nucleoli and necrotic background in these cases (picture 25). Cells exhibited high N:C ratio, nuclear overlapping and crowding, coarse chromatin, prominent macronucleoli in 13 cases [32.50%] and conspicuous nucleoli in 27 cases [67.50%] along with irregular nuclear contours, moderate to significant anisonucleosis (picture 26) and scant to moderate amount of cytoplasm. Drunken honeycomb pattern was noted in 18 [45.00%] of the smears with presence of tumor diasthesis. Many binucleated and

multinucleated cells were also seen. Few of the cases also showed intracytoplasmic neutrophils, which suggests high grade tumor along with mitotic activity (picture 27 and 28). Cytoplasmic vacuolization were also evident with occasional cell showing nuclear budding (picture 29). In our study, we analyzed the constellation of morphological features favouring malignant process seen as drunken honeycomb appearance, prominent macronucleoli, nuclear enlargement with nuclear overlapping and crowding along with significant anisonucleosis. Among all these features, presence or absence of prominent macronucleoli and significant anisonucleosis help in differentiating and categorizing lesions into Suspicious and Malignant.

Out of 40 lesions diagnosed as positive or malignant, trucut biopsies were available in 34 of cases [85.00%] and immunohistochemical studies were done in 14 cases [35.00%].

In 37 cases reported as adenocarcinoma on Cytology, histo-pathological examination was done in 32 cases amongst which 27 cases were diagnosed as adenocarcinoma on histology (picture 31).

Trucut biopsy of 2 cases out of 37 were done and reported as chronic pancreatitis on histopathology, which showed areas of fibrosis with loss of pancreatic acini and lymphocytic infiltrate. Sections showed distorted ductal profiles with ectasia. The cuboidal epithelium lining the ducts displayed reactive changes. Periductal chronic inflammation was seen with intraluminal protein plugs. However there was no evidence of malignancy on histopathology. On reanalyzing the cytology of these two cases, there was lack of marked anisonucleosis and prominent nucleoli. But due to presence of nuclear overlapping and crowding with necro-inflammatory background, these two cases were reported as malignant on cytology. These two cases showed discordance.

On follow up, 4 patients underwent Whipple’s procedure for carcinoma pancreas and were reported ductal adenocarcinoma- moderately differentiated. 7 patients died due to the disease process and data of rest of the cases was not available for follow up.

1 case was diagnosed as Malignant round cell tumor- lymphoma on cytology which showed cellular smears composed of singly dissociated

monotonous population of medium to large round atypical lymphoid cells with high N:C ratio, fine chromatin, conspicuous nucleoli and moderate cytoplasm with vacuolization (picture 32). Background showed lymph glandular bodies along with presence of foamy macrophages (picture 33). It was in concordance with histological diagnosis of Non-Hodgkins lymphoma which showed sheets of medium sized tumor cells having vesicular nuclei, fine chromatin, conspicuous nucleoli and scant amount of cytoplasm. IHC was done in this case which was positive for LCA, CD20, CD10 and Bcl 6 and c-myc. MiB1 was 98% in highest proliferating areas and diagnosis of Non-Hodgkins lymphoma B cell type (high grade), favoring Burkitt's lymphoma was made (picture 34, 35, 36 and 37).

Table 21- Diagnostic spectrum of lesions in category VI- Positive or Malignant Category- Adenocarcinoma [n=39]

Cytological diagnosis [n=39]	**Cytological features**			**Radiological findings [n=30]**	**Histological diagnosis [n=33]**
Adenocarcinoma [n=39]	Architecture	Drunken Honeycomb	18	Mass lesion- likely primary with mitotic activity. Few of the cases also showed marked dilatation of the main pancreatic duct with obstructive biliopathy along with few cases showing strictures in pancreatic duct with adjacent fibrosis [n=30]	Ductal adenocarcinoma [n=27]
		Papillaroid clusters	3		
		Three dimensional clusters	10		Chronic pancreatitis [n=2]
		Singly scattered	39		Inadequate for opinion [n=4]
	Anisonucleosis	4:1	31		
		3:1	8		
		Prominent nucleoli	13		
		Conspicuous nucleoli	26		
	Background	Mucin (both intracellular and extracellular)	2		
		Necrosis	32		

Table 22- Diagnostic spectrum of lesions in category VI- Positive or Malignant Category- Lymphoma [n=1]

Cytological diagnosis [n=1]	Cytological features	Radiological findings [n=1]	Histological diagnosis [n=1]
Malignant round cell tumor- possibly Lymphoma [n=1]	Large atypical lymphoid cells in background of lympho-glandular bodies and foamy macrophages.	Peripancreatic fat inflammation with collection.	Non-Hodgkins lymphoma- B cell type, high grade favoring Burkitts Lymphoma [n=1] LCA- Positive CD20- Positive CD10- Positive Bcl 6- Positive Mib 1- 98% in highest proliferating area. c-myc- Positive

Table 23- Summary of Cytology and Histology correlation [n=70]

Categories	Cytological cases	Histological cases	Histology diagnosis	Risk of malignancy %
Category I- Non Diagnostic	2	1	Adenocarcinoma [n=1]	Not significant
Category II- Negative (for malignancy)	10	1	Fat Necrosis {n=1]	Not significant
Category III- Atypical	3	2	Adenocarcinoma [n=2]	100.00%
Category IV- Neoplastic (Benign or Others)	5	3	Adenocarcinoma [n=1]	33.33%
			Neuroendocrine tumor [n=1]	
			Chronic pancreatitis [n=1]	
Category V- Suspicious (for malignancy)	10	7	Adenocarcinoma [n=7]	100.00%
Category VI- Positive or Malignant	40	30	Adenocarcinoma [n=27]	93.33%
			Chronic pancreatitis [n=2]	
			Non Hodgkins lymphoma-High grade B cell type favouring Burkitts lymphoma [n=1]	

Concordant and discordant cases-

Total of 3 discordant cases were analyzed after cyto-histological correlation. 1 case belonged to category IV (Neoplastic:Others) that showed features of chronic pancreatitis on histology. 2 cases reported as adenocarcinoma on cytology were reported chronic pancreatitis on histology. Rest all the cases being reviewed on cyto-histology correlation were concordant with each other.

Table 24- Summary of concordant and discordant cases

Category	**Cytological diagnosis**	**Histological diagnosis**
Category IV (neoplastic:others)	Pancreatic neuroendocrine tumor	Chronic pancreatitis
Category VI [n=2]	Adenocarcinoma [n=2]	Chronic pancreatitis [n=2]

Chronic pancreatitis was the most misinterpreted lesion in our study.

DISCUSSION

Pancreas is a retroperitoneal, transversely oriented organ extending from shaped loop of duodenum to the hilum of pancreas. The lesions are divided into benign and malignant. Therefore the pancreatic cytopathology plays an important role in diagnosis and management of patients with solid and cystic lesions. Pre-operative diagnosis of pancreatic masses is a challenging task owing to the non-specific clinico-radiological signs and technical difficulty in performing FNAC. FNAC can be performed by a gastroenterologist by endoscopic technique or by an interventional radiologist under CT/USG guidance. Endoscopic ultrasound guided fine-needle aspiration is a minimally invasive technique for the biopsy of pancreatic cysts and mass lesions. It allows the easy and adequate sampling of the tissue with minimal post procedural effects. It also allows the rapid onset evaluation to look for the adequacy of the material being aspirated.

Age and Sex prevalence:

In our study, the age of patients ranged from 10 to 88 years among which the highest number of cases belonged to age group of 51 to 60 years comprising of 40.00%. Only one case each belonged to age group of 1-10 and 21-30 years while none of patient belonged to age group of 11-20 years and 31-40 years. The youngest patient was 10 years old and eldest was of 88 years. The mean age was 60.14 years in our study. The overall incidence was higher in males in our study constituting 71.42% [n=50] of all patients with male to female ratio was 2.5:1. In a study done by Ilyas AM et al, the mean age was 51 years with male predominance. The male to female ratio in his study was 2:1[84]. In a cohort study of 322 cases done by Hoda RS et al males were more commonly affected comprising of 52.2% and females were 47.8%. The male to female ratio was 1.09:1. Patient's age ranged from 18 to 91 years with mean age of 66.1 years. [83] Another concordant study of 101 patients done by Eloubeidi MA et al[85] showed male predominance in pancreatic lesions with male to female ratio of 2:1. The mean age was 62 years with range of 34-89 years. There was

concordance in age and sex prevalence with above mentioned studies however, there were also some studies which showed discordance on the basis of demographics.[85] A study of 223 patients done by Hank M et al showed that pancreatic lesions were more common in females comprising 115 cases [51.56%] with median age of 64 years. The age of presentation ranged from 18-88 years.[88] Another study of 1017 cases done by Sung S et al[82] showed that majority of the patients were female with male to female ratio of 1:1.6 . The age ranged from 15-95 years with median age of 67 years. In study of 69 pancreatic FNA, conducted by Afify AM et al[86] ,there was female predominance with 38 cases and 31 were males and mean age was 65 years. Wright PK et al studied 111 pancreatic FNA cases and showed that female were more commonly involved comprising of 53.15% of all cases [89]. The range of age of patients was 22-83 years with mean age of 63 years. In a study done by Sung S et al, data from 856 patients was collected out of which a total of 1017 pancreatic FNA were studied. Out of these females comprised of 53.00% of all cases and males were 47.00%. the age range in this study was 15-96 years with mean age of 67 years. Analysis of these studies showed that the age group affected is comparable in all studies, however heterogeneity in gender and age is seen in different geographical areas.

Clinical presentation of the cases:

The lesions were analyzed according to the clinical presentation including symptoms and signs. In our study, pain abdomen was the most common presenting symptom constituting 98.57% followed by loss of weight and appetite with jaundice. These symptoms were in concordance with studies done by Ilyas AM et al whose study also showed that pain abdomen and jaundice were the most common symptoms. Another study done by Sung S et al also showed similar clinical features.

Site of pancreatic lesions:

In our study, the most common site of pancreatic lesion was head of pancreas comprising of 61.42% of all the cases followed by body of pancreas. Uncinate process was the least common site involved. Our

findings were in concordance with study done by Ilyas AM et al and Nishith N et al which showed that head of pancreas was most commonly involved site comprising 48% and 42% respectively of all the cases followed by body and least frequently involving the tail of pancreas comprising 12% and 9% respectively. Another study done by Hoda RS et al also showed that head of pancreas was the most common pancreatic site involved, followed by body and least commonly involved part was uncinate process comprising 2.7% of all cases. Study of 101 patients done by Eloubeidi MA et alalso showed concordance with our study in which he found that 67% of the lesions were seen in head of the pancreas with minimum of 6% in tail of pancreas. [85] Our results were also in concordance with study done by Hank M et alwhich showed maximum involvement of head of pancreas by the disease process. On analyzing all the various studies, head of the pancreas remained the most commonly involved area with uncinate process being the least commonly involved in majority of the studies. [88]

Mode of FNAC:

In our study majority of the patients underwent ultrasound guided FNA comprising of 77.14% while 22.85% underwent endoscopic USG guided FNAC. In a study done by Ilyas et al all the patients underwent endoscopic USG guided FNAC and were then categorized further. As in study done by Ilyas et al, the study done by Eloubeidi et al, all the patients underwent endoscopic USG guided FNAC. None of the patient in both these studies underwent USG guided FNAC. Fewer number of endoscopic USG guided FNA in our study can be attributed to the procedure being more expensive and to the fear of endoscopy amongst patients.

Radiological spectrum of lesions:

In our present study, radiological analysis was done in 75.71% [n=53] of the cases. 51 [96.22%] cases out of 53 were reported as solid lesions in imaging and 2 cases [3.77%] were cystic. In study done by Sung S et al, out of 1017 cases, 42.18% cases were cystic in nature and 57.82% were solid. In a study done by Hoda et al, 51.2% cases

were cystic with 48.8% showing solid lesion on imaging. Wright PK et al studied 120 pancreatic FNA cases among which 79 [65.83%] were solid lesions and 41 [34.16%] were cystic lesions.

The Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary cytology represents as important step in diagnosing and categorizing the pancreatic lesions. It is six tier system with risk stratification comprising of Category I- Non diagnostic, Category II- Negative for malignancy, Category III- Atypical, Category IV- Neoplastic, Category IV- Benign, Category V-Suspicious and Category VI- Positive or Malignant.

Table 25 - Category wise distribution of cases in various studies

Category	**Present study (2020-2022)**	**Layfield LJ et al[87] (2004-2014)**	**Nishith N et al[80] (2008-2019)**	**Mancera MS et al[81] (2010-2019)**	**Sung S et al[82] (2014-2020)**	**Hank M et al[88] (2016-2018)**	**Ilyas AM et al[84] (2017-2019)**
	n=70	n=317	n=581	n=297	n=1017	n=223	n=60
I	2 [2.85%]	14 [4.41%]	50 [8.60%]	30 [10.10%]	242 [23.79%]	50 [22.42%]	7 [11.60%]
II	10 [14.28%]	103 [32.49%]	175 [30.12%]	45 [15.15%]	162 [15.92%]	43 [19.28%]	16 [26.60%]
III	3 [4.28%]	23 [7.25%]	19 [3.27%]	20 [6.73%]	142 [13.96%]	14 [6.27%]	1 [1.60%]
IV-Benign	-	14 [4.41%]	27 [4.64%]	-	20 [1.96%]	12 [5.38%]	-
IV-Others	5 [7.14%]	-	30 [5.16%]	42 [14.14%]	133 [13.07%]	55 [24.66%]	9 [15.00%]
V	10 [14.28%]	22 [6.94%]	26 [4.47%]	19 [6.39%]	28 [2.75%]	15 [6.72%]	8 [13.30%]
VI	40 [57.14%]	141 [44.47%]	254 [43.71%]	141 [47.47%]	290 [28.51%]	34 [15.24%]	19 [31.60%]

In the present study, cytological categorization of 70 cases was done according to the Papanicolaou Society of Cytopathology System for Reporting Pancreaticobiliary cytology. In our study, category VI (positive or malignant) was the most common category comprising of

57.14% followed by category V and category II each comprising of 10 cases [14.28%]. The least common category diagnosed was non diagnostic comprising of only 2 cases [2.85%]. None of the case belonged to Neoplastic:Benign category.

Correlating our study with other studies as shown in table 25, Category VI (positive or malignant) was the most common catgeory in pancreatic cytology except for study done by Hank M et al[88] who in his study showed majority of the cases belonged to Neoplastic:Others category (IVb) comprising of 24.66% of all the cases [n=55] followed by non diagnostic category. 15.24% cases were analyzed and belonged to positive or malignant.

In our study along with studies done by Ilyas AM et al ,there was no case belonging to category IVa (neoplastic:benign), which can be attributed to small sample in both these studies. Also our study was performed during COVID 19 pandemic which is responsible for overall smaller number of cases.

Category I- Non diagnostic [n=2, 2.85%]

In our present study, 2.85% of the cases [n=2] were categorized under the Non-diagnostic category which was least in number among all cases. One lesion was seen in head of pancreas and other in uncinate process. Both the patients were male and underwent endoscopic USG guided procedures. One of the case in our study showed mainly hemorrhage with few scattered foamy macrophages with background of thin extracellular mucin while other cases showed only mucin. No epithelial cell was found in both the smears. Histopathological examination was done in only one case which was discordant and showed features of adenocarcinoma on trucut biopsy. Nishith N et al analyzed 581 cases out of which 8.60% cases belonged to Non Diagnostic category. He explained that lack of epithelial component and hemorrhagic background was the most common reason for Non Diagnostic.[80] Study of 317 pancreatic FNA cases done by Layfield LJ showed that only 4.41%[n=14] cases were reported as non diagnostic. This is in variance with studies done by Mancera MS et al, Sung S et al, Hank M et al and Ilyas AM et al who analyzed 10.10%, 23.79%,

22.42% and 11.60% of cases as Non Diagnostic. The low number of cases in Non Diagnostic category in our study is explained by rapid on site evaluation of the sample done for most of the samples. Rapid on site evaluation is a valuable tool in accessing the diagnostic accuracy of the sample obtained during pancreatic FNA. It is a protocol in our institution, hence the low number of Non diagnostic cases is attributed to it. If the cellularity is suboptimal on rapid on site evaluation, then the procedure is usually repeated if the patient is cooperative. Both the cases of Non-diagnostic category underwent endoscopic USG guided FNA. The maximum number of cases in non diagnostic category belonged to study done by Sung S et al which comprises of 23.27% of all cases. Hank M et al showed 22.42% cases were reported as non diagnostic due to insufficient cellularity.[88]

Risk of malignancy in category I is not significant in our study as the sample size is low with only 2 cases belonging to non diagnostic category. Histo-pathological correlation was seen in only one case which was further reported as adenocarcinoma. Other studies done by Hoda RS et al, Layfiled LJ et al and Wright PK et al showed absolute risk of malignancy as 7.7%, 21.4% and 33.3% respectively.

Category II- Negative (for malignancy) [n=10,14.28%]

A total of 14.28% [n=10] cases were reported as Negative (for malignancy) in our study. Out of 10 cases in category II, 20.0% [n=2] cases were reported as granulomatous inflammation in which 20% ZN stain for AFB was done and was found to be non-contributory. One case was reported as pseudocyst as it showed necrotic debris with crystals, foamy macrophages and scattered inflammatory cells. Another case was reported as benign cystic lesion as it showed sheets and clusters of benign epithelial cells against a fluidy background. 60.0% [n=6] cases were reported as non diagnostic without further categorization. In a study by Ilyas AM et al, 26.6% [n=16] cases were reported as Negative (for malignancy), amongst which one case was of granulomatous inflammation and fourteen cases were reported as pseudocyst. Nishith N et al in his study reported 30.14% cases as Negative with most having a descriptive diagnosis without any further

subcategorization followed by pancreatitis comprising 10.2% of all cases and granulomatous pancreatitis comprising 4.5% of all cases. Our study was comparable with studies done by Mancera MS et al who showed similar percentage of patients under this category which was 15.15% and Sung S et al who showed 15.92% cases were categorized under this. Sung S et al explained in his study that presence of sheets of benign cells without any atypia or mucin was the reason of his diagnosis.[82]

Absolute risk of malignancy in our study for Negative category was not signficant as only one patient underwent histo-pathological examination. This was in concordance with study done by Ilyas et al. Absolute risk of malignancy was 1.0%, 12.6% and 8.3% in studies done by Hoda etl, Layfield et al and Wright et al respectively.

Category III- Atypical [n=3, 4.28%]

Aspirations which lacked either qualitative or quantitative cytomorphological features to be diagnosed as nonneoplastic or neoplastic are categorized under atypical. In our study, only 4.28% [n=3] cases belonged to Atypical category. All the three lesions were in body of pancreas and presented with mass lesion on radiology. 1.60% cases were reported as atypical in study conducted by Ilyas AM et al, while Sung S et al reported 13.92% cases, Nishith N et al reported 6.73% cases and Layfield LJ et al reported 7.25% cases as atypical. Study done by Afify AM et al reported 8.69% cases as atypical and Eloubeidi MA et al categorized 5.94% cases as atypical.

In our study, the smears showed cohesive clusters and monolayered sheets of ductal epithelial cells exhibiting mild degree of nuclear atypia with high N:C ratio, insignificant anisonucleosis, inconspicuous nucleoli, nuclear overlapping and crowding with focal irregularity of cell membranes with background showing mucin, however it was devoid of necrosis in all the three cases. Ilyas AM et al reported only one case as atypical in which he saw few atypical cells with benign epithelial cells which on biopsy revealed an inflammatory reaction.[84] In study done by Sung S et al, the most common reason for atypical category was low cellularity or scant mucin like material with presence of abundant

inflammation and poorly preserved cells.[82] Nishith N et al studied 19 cases [3.27%] of atypical cases which reported on the basis of presence of few atypical cells which were neither fulfilling the criteria of neoplasm, nor of non neoplastic condition. In his study histological analysis was present in only 3 cases, among which 2 showed no evidence of any granulomatous inflammation or malignancy while one showed features of adenocarcinoma.[80]

In our study 3 cases were diagnosed as atypical on cytology, out of which histo-pathological evaluation was done in 2 cases and both were reported as adenocarcinoma on follow up and/or histology. Absolute risk of malignancy was 100.0% in atypical category. In study done by Ilyas AM et al, there was only one case diagnosed as atypical for which follow up was not available, therefore ROM was nil in his study. Studies done by Hoda RS et al, Layfield LJ et al and Wright PK et al showed ROM as 28.0%, 73.9% and 100% respectively. According Papanicolaou Society of Cytopathology for reporting pancreatobiliary cytology, the risk of malignancy for solid lesions in atypical category is 82-86% for endoscopic USG guided FNAC.[90-93]

Category IV- Neoplastic [n=5, 7.14%]

7.14% [n=5] cases belonged to Neoplastic category. All the 5 cases were categorized into Neoplastic:Others. None of the case in our study was reported as Neoplastic:Benign. This was in concordance with studies done by Ilays AM et al who showed no case under Neoplastic:Benign group. Though the sample size was 297 in study done by Mancera MS et al, none of the case was categorized under neoplastic:benign category.

In our study, four of these cases were males and 1 was female. They all presented with pain abdomen. Head of the pancreas was the most common site involved under neoplastic category accounting for 80.00%. In our study, 2 cases were reported as mucinous cystic neoplasm, 2 cases as pancreatic neuroendocrine tumor of pancreas and 1 case was of pancreatic pseudopapillary neoplasm. Histo-pathological examination was done in 3 cases in which one case of mucinous cystic neoplasm was found to be adenocarcinoma on

histology. SPEN on cytology was found to be neuroendocrine tumor of pancreas on histology which was further proven on IHC. Immunohistochemical findings showed that tumor cells were immunopositive for CK-7, CK-20, CDX-2, synaptophysin, dot positivity for chromogranin and negative nuclear staining for beta-catenin. Neuroendocrine tumor is a close differential on SPEN and there is morphological overlap in both the conditions. As both neuroendocrine tumor and pancreatic pseudopapillary neoplasm belongs to same category, it was not considered as the discordant case. Other case reported as neuroendocrine tumor on cytology was found to chronic pancreatitis on histology. The reason for discordance was large number of pancreatic acinar cells displaying reactive atypia which were over-read as neuroendocrine tumor on cytology.[94] Ilyas AM et al in his study also showed that total of nine cases [15.00%] were diagnosed as neoplastic:others out of which three [33.3%] were solid pseudopapillary epithelial neoplasm while six [66.6%]were pancreatic neuroendocrine tumor[84] which were concordant with the histo-pathological findings.

In another study by Sung S et al, a follow up data of 133 patients was available in neoplastic:others category amongst which 50.37% [n=67] cases had a diagnosis of mucinous cystic neoplasm showing similar features as in our study seen as clusters of atypical cells displaying anisonucleosis present against as mucinous background.[82]

In Neoplastic:Benign category, the absolute risk of malignancy was not significant as there was no case analyzed in this category. This was in concordance with study done by Hoda RS et al, in whose study, there was also no case belonging to Neoplastic:Benign category. However, the absolute risk of malignancy in Neoplastic:Benign category among studies done by Layfield LJ and Wright PK et al were 14.2% and 66.7% respectively.

In Neoplastic:Others category of our study, histo-pathological examination was done in 3 cases and 1 was found to malignant. Therefore absolute risk of malignancy was 33.3%. Correlating with other studies, absolute risk of malignancy was 30.0%, 100.0% and

34.3% in studies done by Hoda RS et al, Wright PK et al and Sung S et al. respectively.

Catergory V- Suspicious for malignancy [n=10, 14.28%]

In our study, 14.2% [n=10] cases were diagnosed as Suspicious for malignancy. Among these, 8 were males and 2 were females with male to female ratio of 4:1. Seven patients had lesion in the head of pancreas. Cases reported as Suspicious for malignancy had some features of malignancy but not all ;moreover these features were focal in nature and confined to few of the clusters. The cells were arranged in three dimensional, cohesive and papillaroid clusters along with singly scattered population with presence of moderate to marked anisonucleosis. The background was necro-inflammatory in three of them. Among 10 cases, histo-pathological examination was done in 8 and among them seven cases were reported as adenocarcinoma and one was given non diagnostic due to inadequate material. In another study done by Nishith N et al, 4.47% [n=26] cases were reported as suspicious for malignancy on cytology and histological examination was present in only one case which was reported as adenocarcinoma[80]. The cytological features in cases reviewd by Nishith N et al were same as of our study. The study done by Ilays AM et al showed 13.30% [n=8] cases belonged to suspicious category with Layfield LJ et al, Mancera MS et al and Sung S et al showing 6.94%, 6.39% and 2.75% of cases of Suspicious category respectively.

Absolute risk of malignancy in our study was 100.0% of suspicious category as all the cases who underwent histo-pathological examination were reported as adenocarcinoma. While comparing it with study done by Ilyas AM et al the risk of malignancy was 87.5%. Further study done by Hoda RS et al showed ROM of 100.0%, while Layfield LJ et al and Wright PK et al showed ROM of 81.8% and 100.0% respectively.

Category VI- Positive (for malignancy) [n=40,57.14%]

Aspirations having cytomorphological features of malignancy were put in this category.

In our study, out of 40 cases 39 [97.5%] cases were reported as adenocarcinoma on cytological examination. The most common age group affected in our study was 51-60 years with 27 males and 13 females. Head of the pancreas was the most common site involved constituting 55.00% of all the cases in this study. This was concordant with all the other studies such as Ilays AM et al, Sung S et al, Mancera MS et al, Nishith N et al and Layfield LJ et al which also showed category VI as the most common category diagnosed according to Papanicolaou society of cytopthalogy system for reporting pancreaticobiliary cytology. In study done by Nishith N et al, males were more involved than females with male to female ratio of 1.2:1. Our study was discordant with study done by Hank M[[88] et al which showed category IVb as the most common category diagnosed.

In our study 39 cases out of 40 were reported as adenocarcinoma on cytology. These cases showed presence of three dimensional, papillaroid clusters along with drunken honeycomb pattern of atypical ductal cells exhibiting marked anisonucleosis in most of the cases with prominent nucleoli and necro-inflammatory background. 1 was diagnosed as malignant round cell tumor-possibly lymphoma which showed medium atypical lymphoid cells with background of lymphoglandular bodies. Histological examination was done in 34 cases, out of which 28 cases were in concordance with initial cytological findings out of which 27 were reported as adenocarcinoma on histology, 1 was reported as lymphoma, 2 were reported as chronic pancreatitis and 4 were inadequate for evaluation due to less cellularity. Risk of malignancy was 93.33% in our study.

In a study of 581 pancreatic samples by Nishith N et al, 43.71% [n=254] cases were diagnosed as category VI. Out of these 254 cases, 90.55% [n=230] were diagnosed adenocarcinoma, 2.3% [n=6] cases were diagnosed as adenosquamous carcinoma, 1.5% [n=4] were mucinous cystadenocarcinoma, 2 were poorly differentiated carcinoma, 1 was small cell neuroendocrine carcinoma and pancreatoblastoma each, 2 were Non Hodgkins lymphomas and lymphoproliferative disorders each and six were metastasis to pancreas. Histological

examination was done in 6.2%[n=16] cases out of which 8 were diagnosed adenocarcinoma and were in concordance with initial cytological diagnosis of adenocarcinoma. One was concordant with Non Hodgkins lymphoma, while 4 were discordant and were diagnosed chronic pancreatitis.

In another study by Ilyas AM et al 31.60% [n=19] cases were diagnosed as category VI, out of which 18 were adenocarcinoma and one was acinar cell carcinoma. Histological examination was done in 17 cases and all were in concordance with the initial cytological findings.

Study by Sung S et al[82] also showed that 28.51% of the cases belonging to category VI were adenocarcinoma of the pancreas and were in concordance with our study.

Absolute risk of malignancy was 93.3% in our study, while comparing with study done by Ilyas AM et al the risk of malignancy was 100% in category VI. Other studies done by Hoda RS et al, Layfield LJ et and Wright PK et al showed ROM as 100.0%, 97.2% and 100.0% respectively which was more as compared to our study.

Table 26- Risk of malignancy in our study

PSRPC	Number of Cases	Cytological diagnosis	Histological diagnosis	ROM (Our study)
Category I	2	Non diagnostic	Adenocarcinoma [1]	Not significant
Category II	10	Granulomatous [2] Pseudocyst [1] Benign cystic lesion [1] Negative for malignancy unclassified [6]	Fat necrosis [1]	Not significant
Category III	3	Atypical	Adenocarcinoma [2]	100.0%
Category IV	5	IV- benign- nil IV- others- • Mucinous cystic neoplasm [2] • Pancreatic solid pseudo-papillary epithelial neoplasm [1] • Pancreatic neuroendocrine tumor [2]	- Adenocarcinoma [1] Neuroendocrine tumor of pancreas [1] Chronic pancreatitis [1]	33.3%
Category V	10	Suspicious	Adenocarcinoma [7]	87.5%
Catgeory VI	40	Adenocarcinoma [39] Malignant round cell tumor- lymphoma [1]	Adenocarcinoma [27] Non Hodgkins lymphoma [1] Chronic pancreatitis [2]	93.3%
Total	70			

Table 27- Comparison of absolute risk of malignancy with other studies

PSRPC	Present study	Hoda RS et al.	Layfield LJ et al.	Wright PK et al.	Ilyas AM et al.	Sung S et al.
Category I	Not significant	7.7%	21.4%	33.3%	-	25.0%
Category II	Not significant	1.0%	12.6%	8.3%	-	17.4%
Category III	100.0%	28.0%	73.9%	100.0%	Nil	41.8%
Category IV- Benign	Not significant	0.0%	14.2%	66.7%	-	0.0%
Category IV- Others	33.3%	30.0%	-	100.0%	-	34.3%
Category V	100.0%	100.0%	81.8%	100.0%	87.5%	95.5%
Category VI	93.3%	100.0%	97.2%	100.0%	100.0%	99.6%

Limitations of the study

The limitations of the study mentioned includes a small sample size. Additionally, the study being conducted at a single center may limit the generalizability of the results to the entire population. Furthermore, the absence of ancillary testing in our study prevented the accuracy in the indeterminate category.

Future perspectives-

To maximize patient care we should evaluate pancreatic aspiration cytology with proper specimen triage for relevant ancillary testing. Cell block preparations with SMAD4 in immunostaining can be helpful and use of next generation sequencing may soon provide a cost effective platform to analyze genetic mutations. In cases of cystic pancreatic lesions, we should try to incorporate cyst fluid analysis with biochemical and molecular testing for mutations in KRAS and GNAS.

SUMMARY AND CONCLUSION

A study was conducted on pancreatic aspirates of 70 patients who underwent fine needle aspiration (FNA) either by endoscopic USG guided or USG guided technique over a period of two years from 1st March 2020 to 28th February 2022 (one year retrospective and one year prospective) in department of pathology in Dayanand Medical college and Hospital Ludhiana.

In every patient, personal history, clinical, biochemical and radiological findings were recorded.

Histological correlation was done in those patients, in whom trucut biopsies were also taken.

Total of 70 cases were analyzed for cytopathological examination and trucut biopsies/ cell blocks were available in 50 patients.

The following conclusions were made:-

1. The maximum cases belong to age group of 51-60 years comprising 40.00% [n=28] of all the cases. Mean age was found to be 60.14 years. The youngest patient was 10 years old and the eldest was 88 years.
2. There male predominance in our study with male to female ratio of 2.5:1.
3. Pancreatic head was most commonly involved site constituting 61.42% [n=43] followed by body of pancreas comprising 25.71% of all cases [n=18]. Uncinate process was least commonly involved site.
4. Maximum number of cases belonged to category VI (positive or malignant).
5. Radiological examination was done in 53 patients and 50 showed malignant lesions on the imaging.
6. Pain abdomen was present in almost all the cases with many patients having overlap with other symptoms like jaundice, loss of appetite and weight.
7. Out of 70 patients, majority of the patients underwent USG guided FNA procedure comprising of 77.14% [n=54].

8. Rapid on set evaluation was done in cases wherever possible.
9. Non-diagnostic category comprised of only two cases, out of which only one case was evaluated on histopathology and was reported as adenocarcinoma. Therefore due to small sample size, the risk of malignancy was not significant.
10. There were total of 10 cases in category II that was negative for malignancy and none of the case was reclassified into malignant on histology or follow up and risk of malignancy was nil .
11. Under the atypical category there were 4.28% of all the cases that either lacked qualitative or quantitative cytomorphological features of neoplastic or non neoplastic category. Risk of malignancy was 100.0% as out of 3, 2 cases underwent histopathology and both were reported as adenocarcinoma.
12. Under Neoplastic category, all our cases were sub classified into Others. The risk of malignancy was 33.33% as histo-pathology was done in 3 cases and 1 was found to be adenocarcinoma.
13. Suspicious for malignancy comprised 10 cases accounting for 14.28% and risk of malignancy was found to be 100.0% as all the cases in which histopathology was done were found to be adenocarcinomas.
14. Adenocarcinoma was overall the most common diagnosis given on cytology and also among category VI. Risk of malignancy in category VI was 93.33%.
15. Positive predictive value in this study is 94.5%.
16. Chronic pancreatitis was the most misinterpreted lesion in our study.

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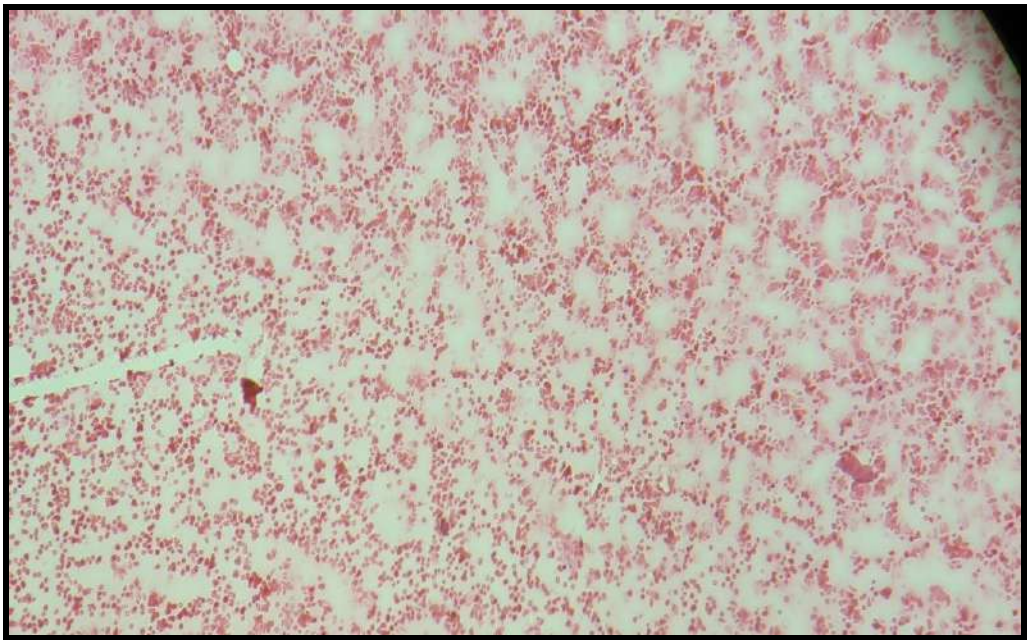
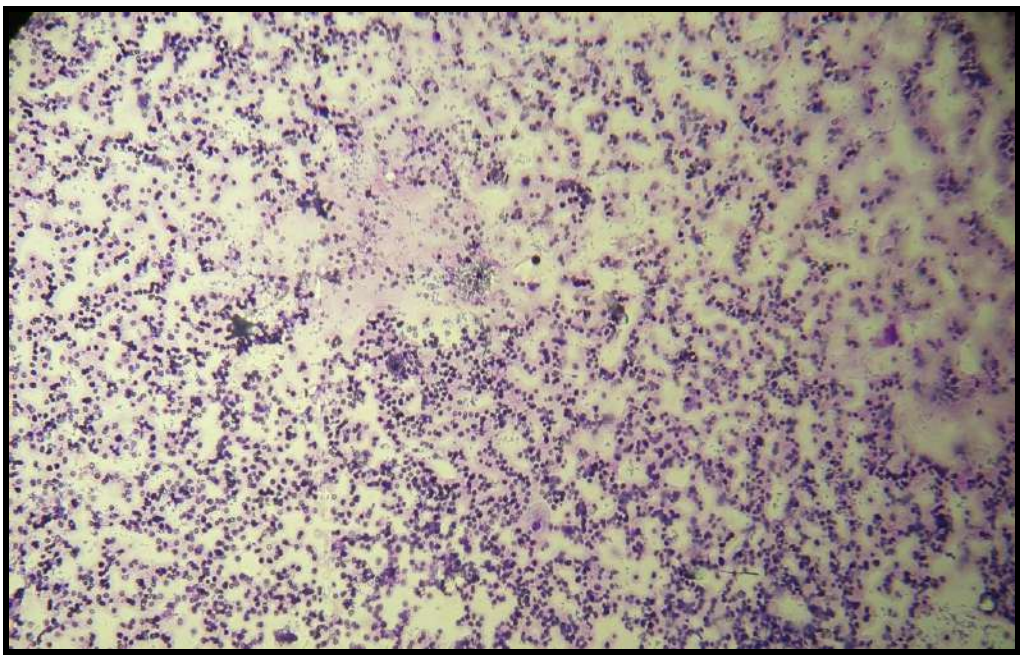
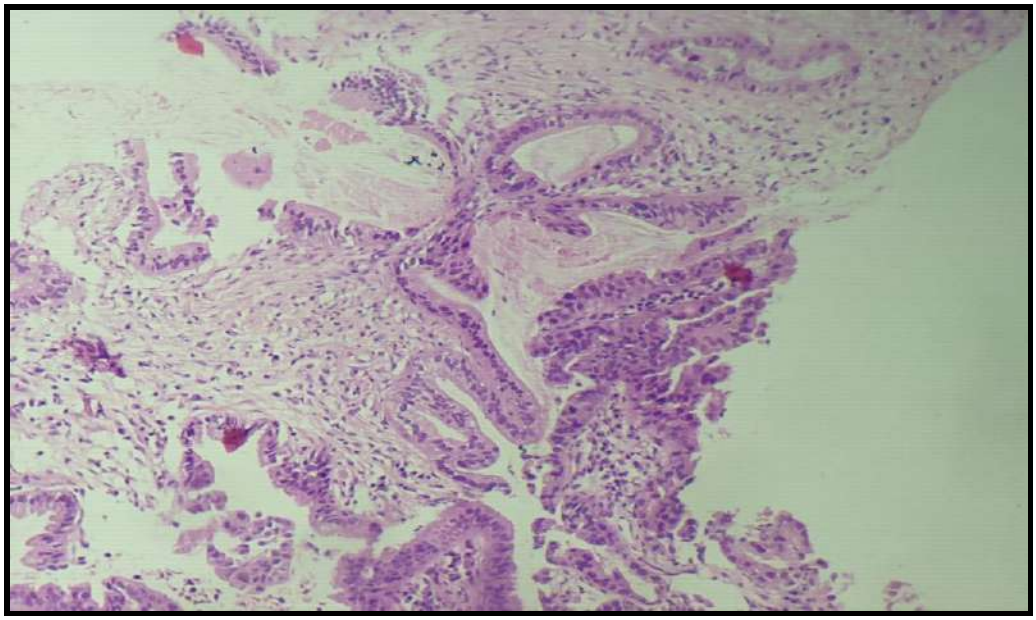


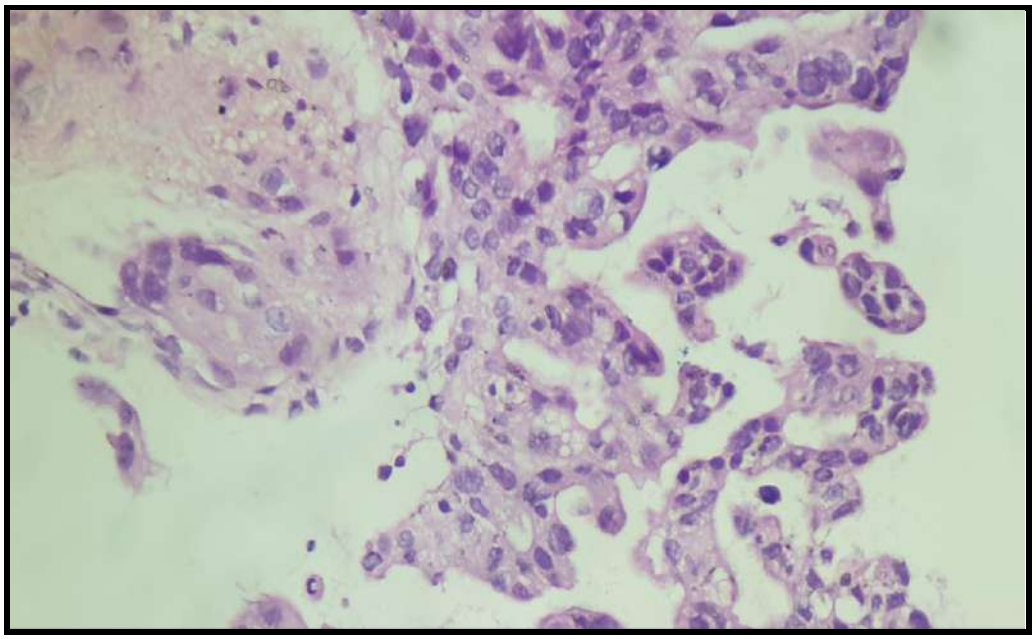
Picture 1- Category I- Non diagnostic.
Photomicrograph shows hemorrhagic background only (H&E 100x)



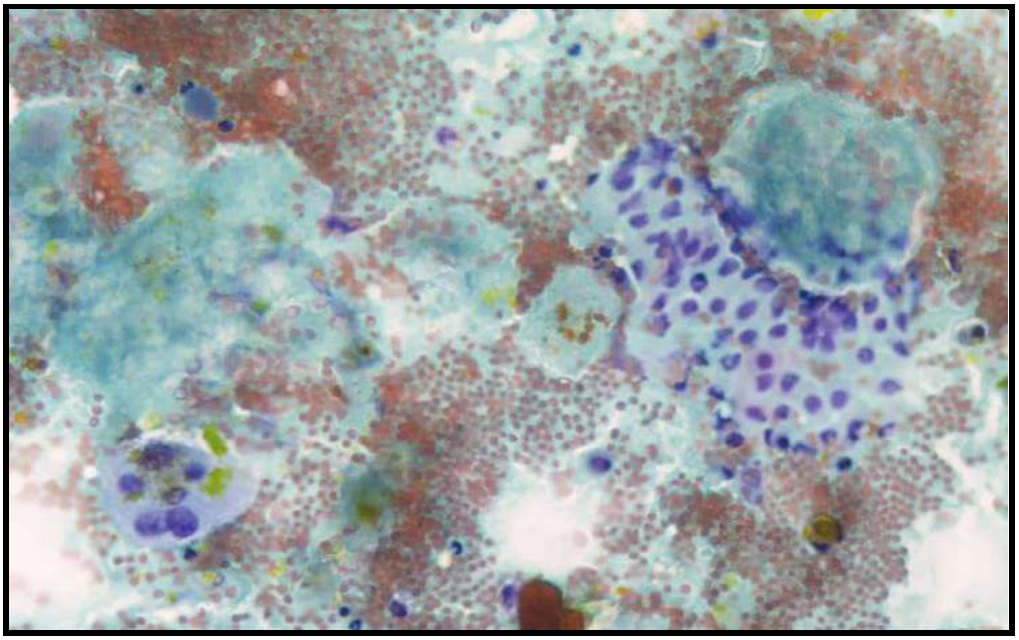
Picture 2- Category I- Non diagnostic
Photomicrograph shows hemorrhagic background with presence of occasional foamy macrophages (Giemsa 100x).



Picture 3- Photo micrograph shows presence of tumor with tumor cells arranged in glandular configuration – Adenocarcinoma (H&E 100x)
Case of Non diagnostic which showed adenocarcinoma- Category I.

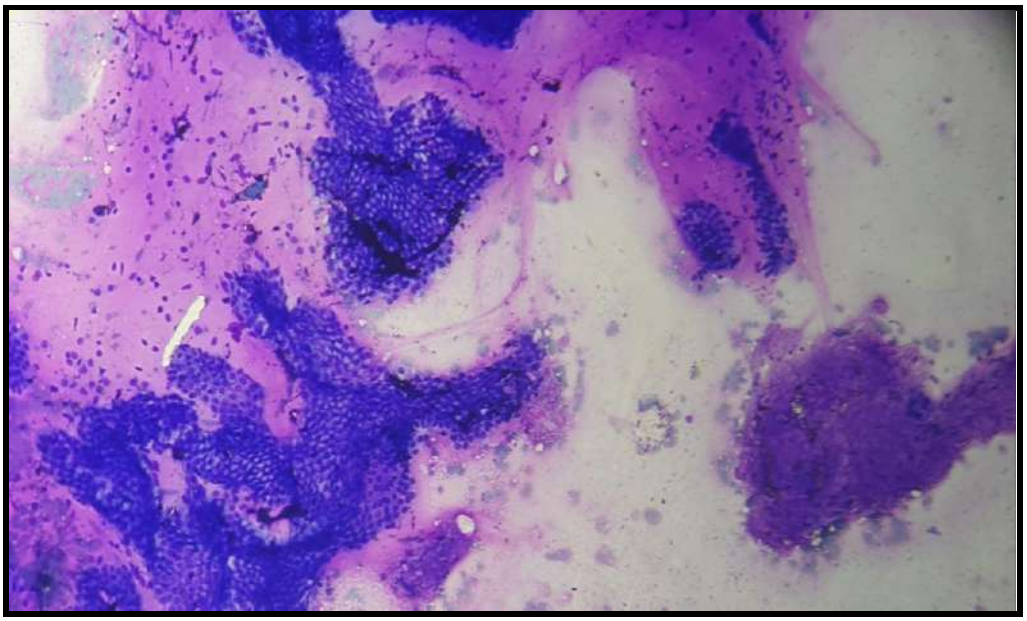


Picture 4- Photomicrograph show glandular arrangement of cells with prominent nucleoli- Adenocarcinoma. (H&E 400x)



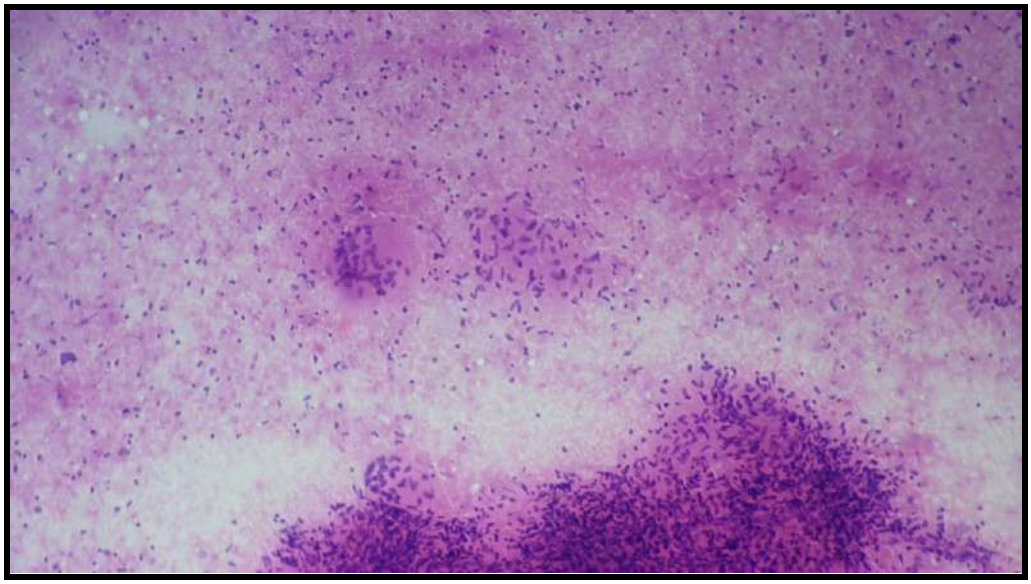
Picture 5- Category II- Negative for malignancy

Photomicrograph shows presence of granular necrotic debris along with yellow pigment, crystals and giant cell-Pseudocyst. (PAP 100x)



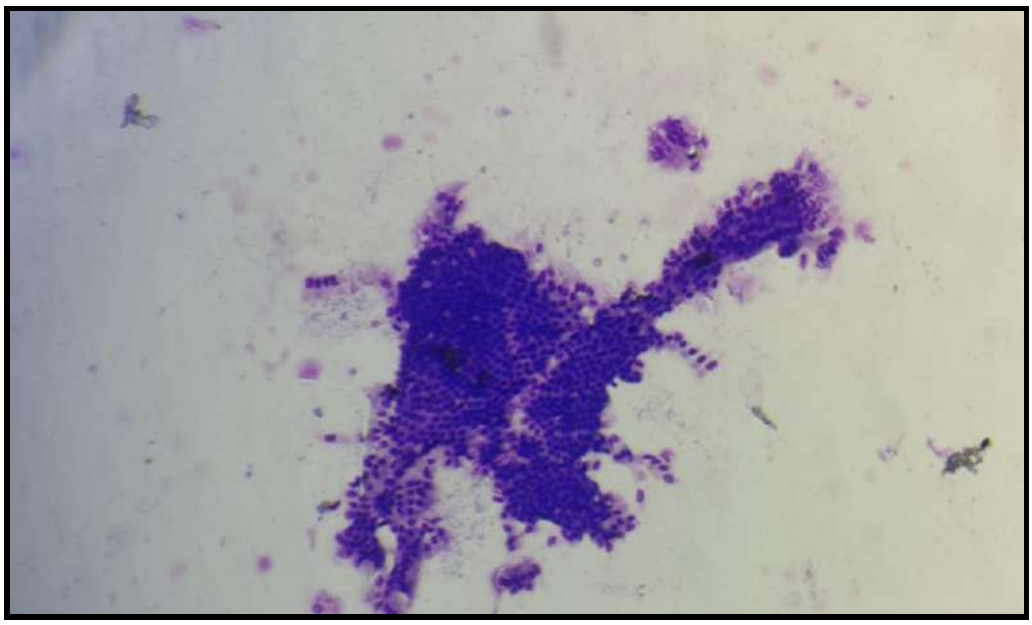
Picture 6- Category II- Negative for malignancy

Photomicrograph shows presence of sheets of benign ductal epithelial cells with few foamy macrophage against a thin fluidy background- Benign cystic lesion (Giemsa 100x)



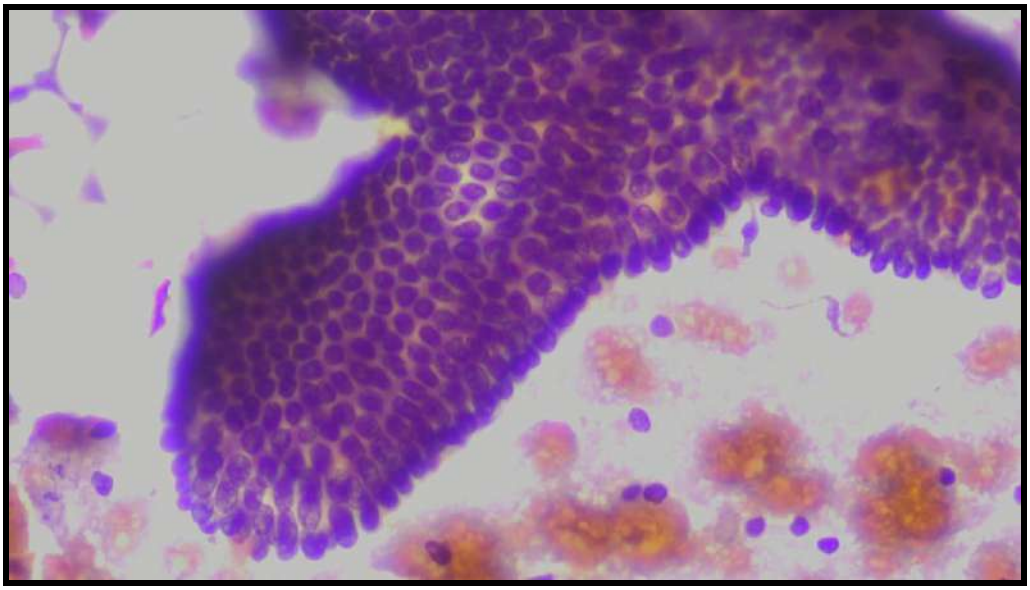
Picture 7- Category II- Negative for malignancy

Photomicrograph show epithelioid cells granuloma with multinucleated giant cell- Granulomatous pancreatitis (Giemsa 100x)

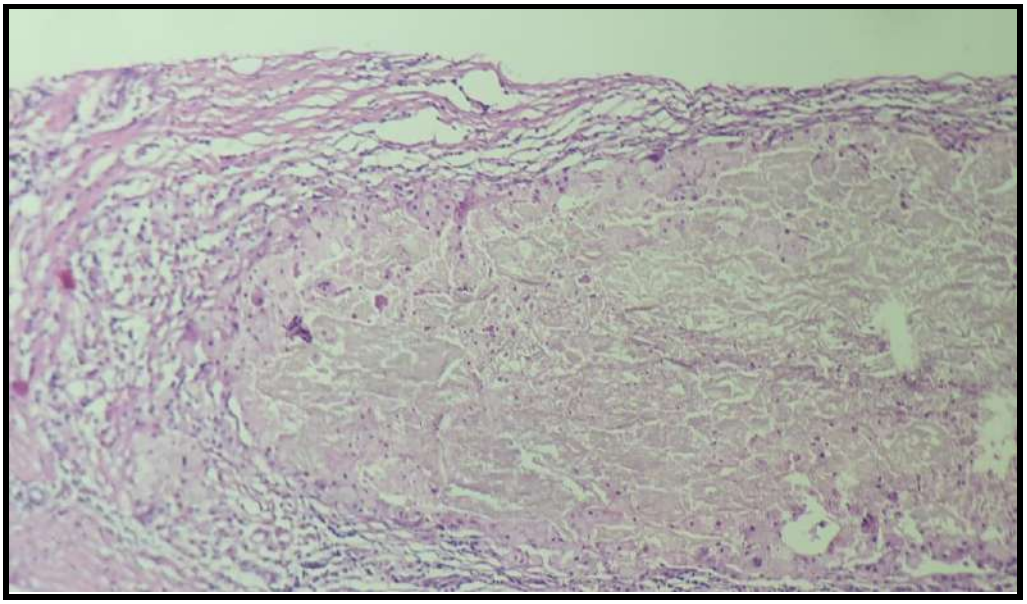


Picture 8- Category II- Negative for malignancy

Photomicrograph shows presence of sheet of benign ductal epithelial cells. No nuclear atypia noted. (Giemsa 100x)

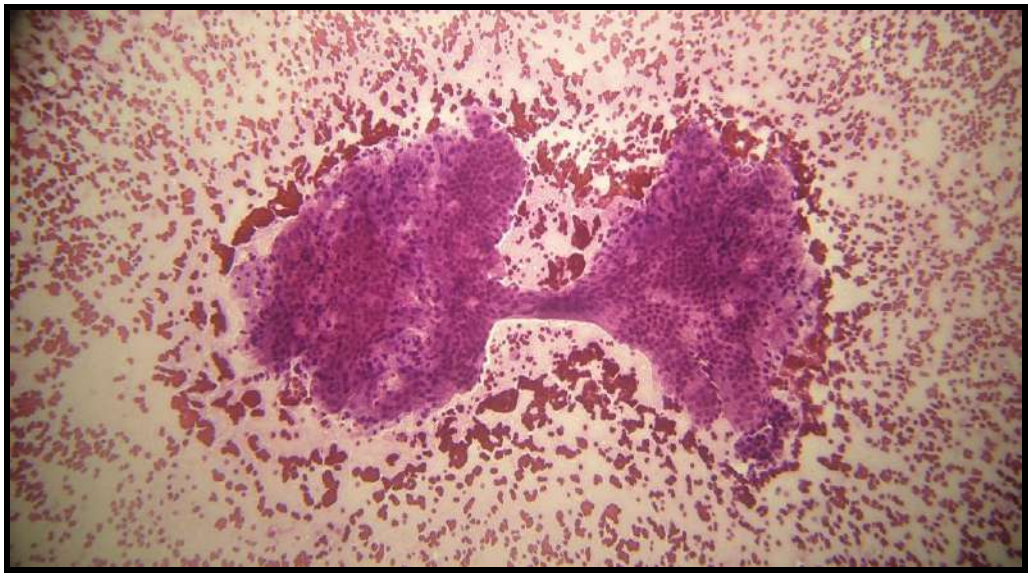


Picture 9- Category II- Negative for malignancy
Photomicrograph shows presence of benign sheet of ductal epithelial cells showing no cytological atypia. (Giemsa 400x)



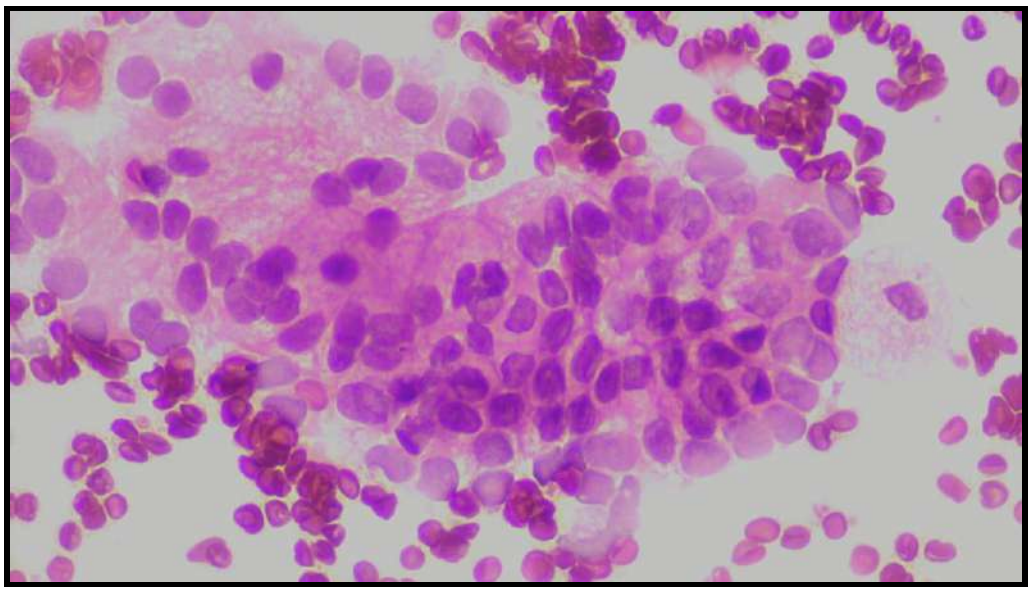
Picture 10- H&E stained section from pancreas show fat necrosis along with background of acute and chronic inflammatory infiltrate.

This case was concordant with cytology on which it was reported as Negative for malignancy.(100x)



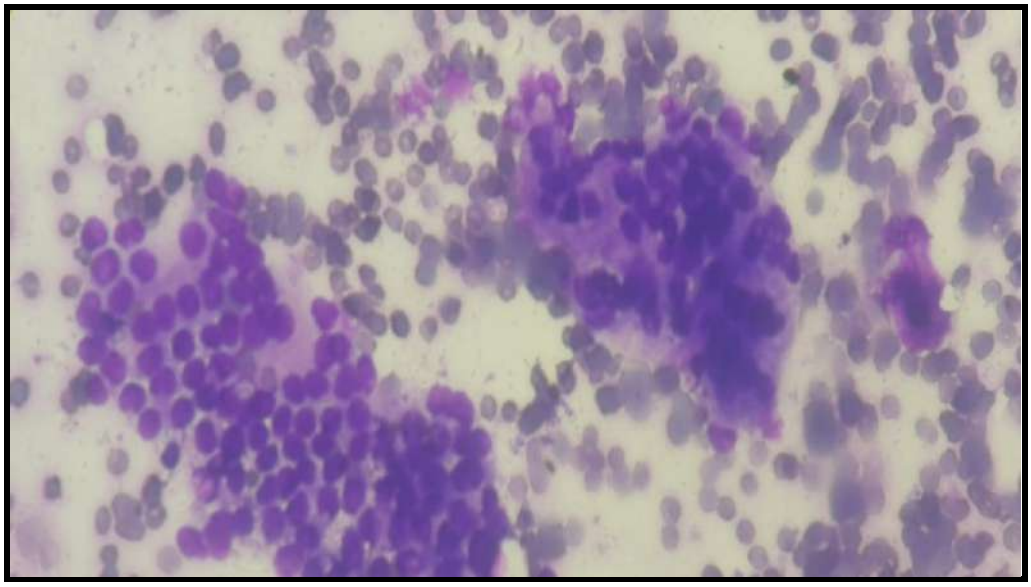
Picture 11- Category III- Atypical

Photomicrograph shows sheets of ductal epithelial cells with focal areas exhibiting nuclear overlapping and crowding. (H&E 100x)



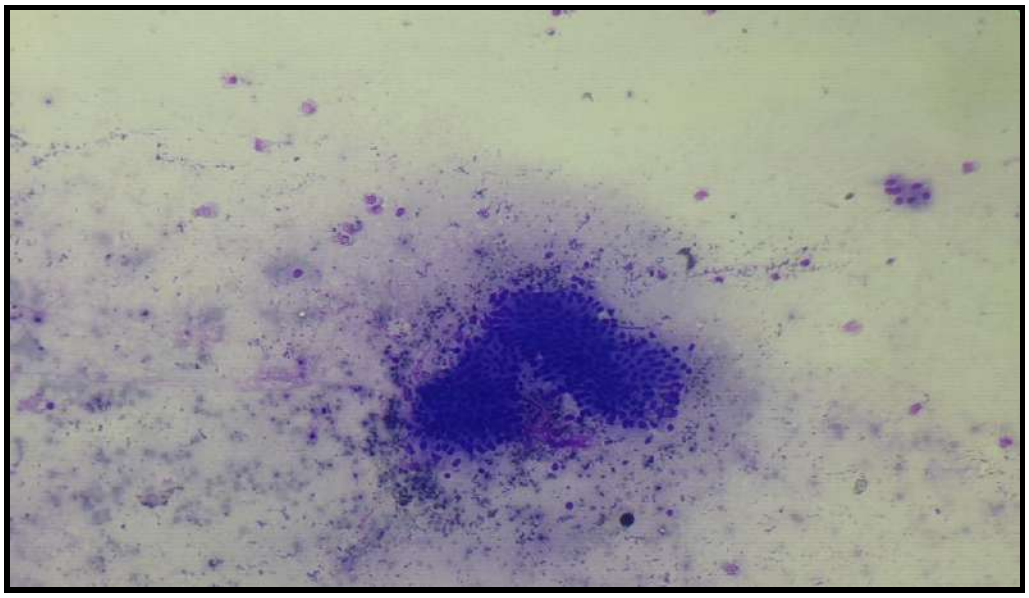
Picture 12- Category III- Atypical

Photomicrograph shows mild anisonucleosis(2:1) with focal area showing nuclear overlapping and crowding. (Giemsa 400x)



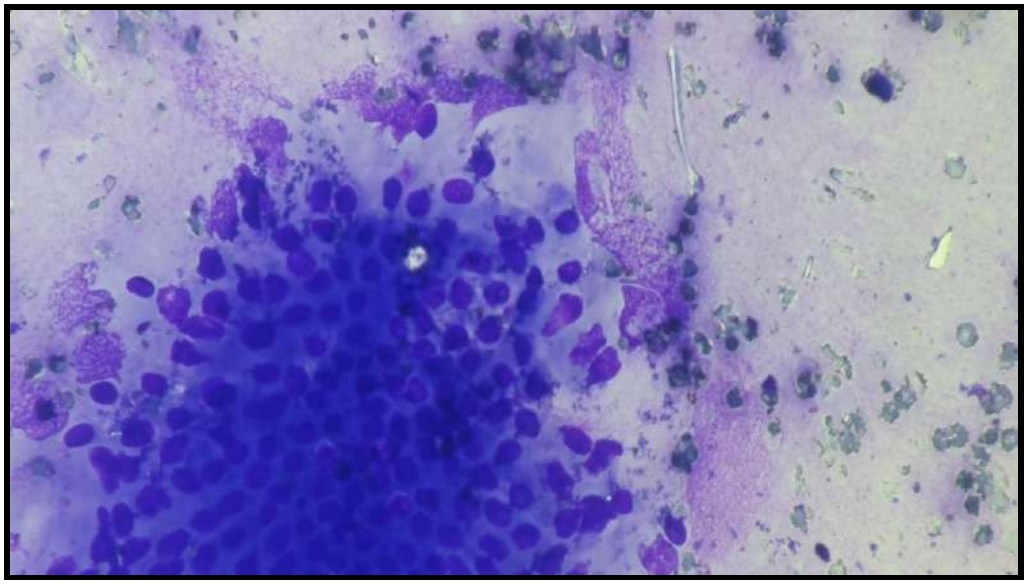
Picture 13- Category III- Atypical

Photomicrograph shows a sheet of benign ductal epithelial cells with adjacent area showing a cluster of cells exhibiting mild nucleo-megaly with nuclear overlapping. Few bare nuclei also noted in background (Giemsa 400x)



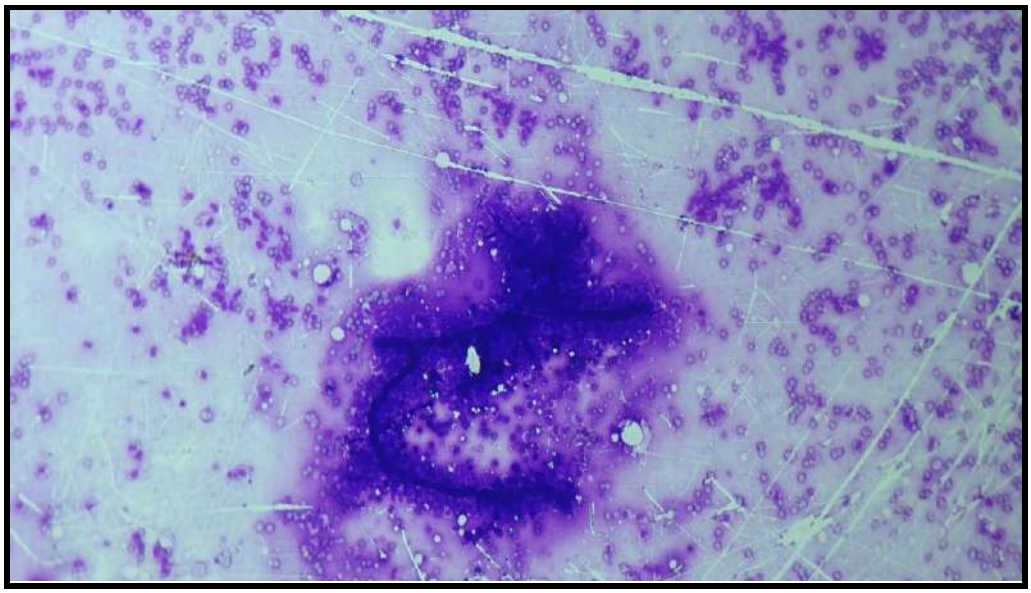
Picture 14- Category IV- Mucinous cystic neoplasm

Photomicrograph shows sheet of bland glandular epithelial cells exhibiting low grade dysplasia present against a mucinous background. (Giemsa 100x)



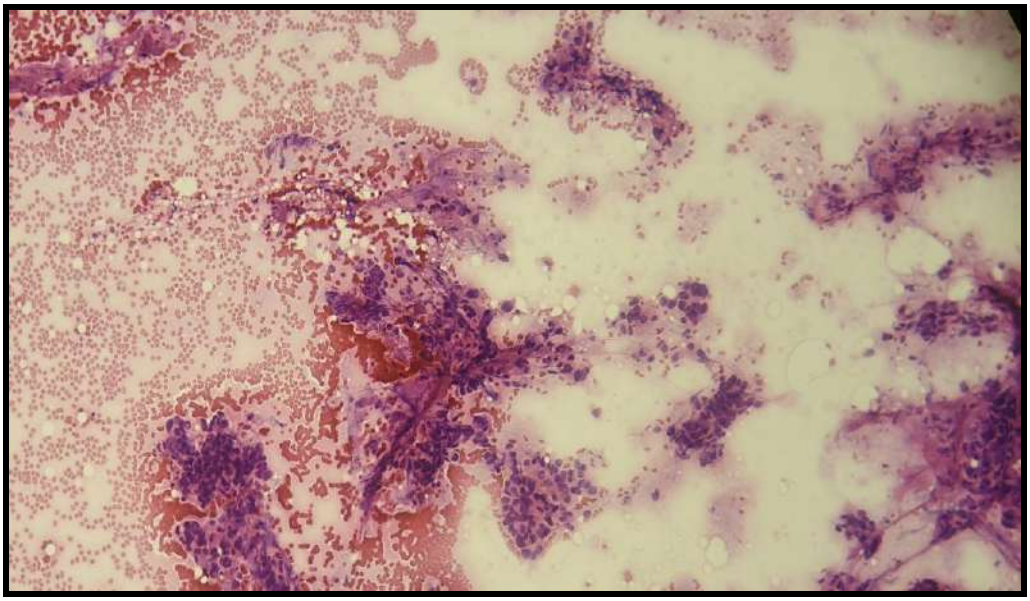
Picture 15- Category IV- mucinous cystic neoplasm

Photomicrograph shows glandular epithelial cells exhibiting low grade dysplasia against a mucinous background. (Giemsa 400x)



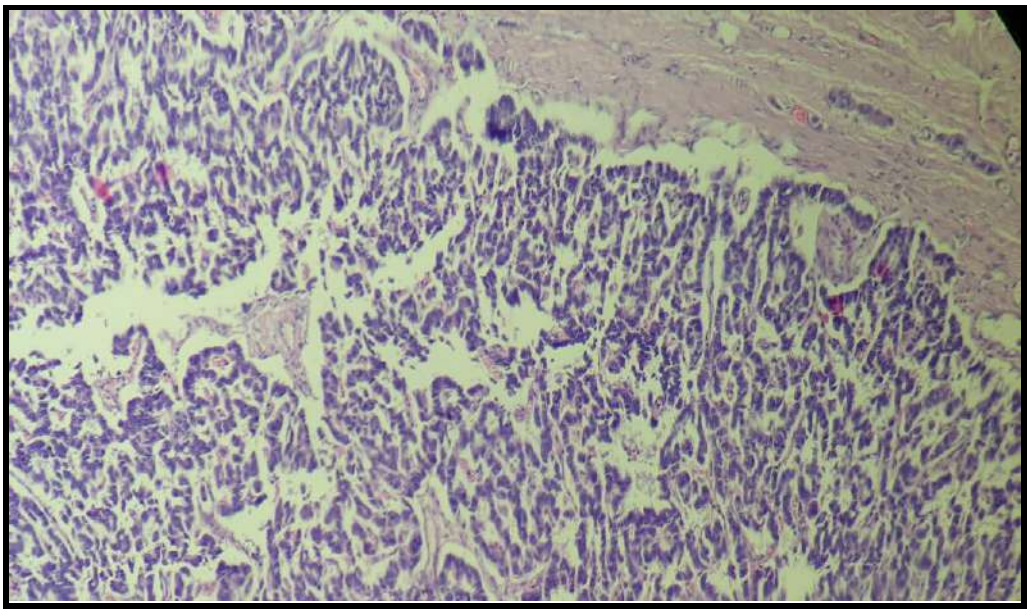
Picture 16- Category IV- Neoplastic

Photomicrograph shows a papillaroid clusters with fibrovascular core composed of mildly pleomorphic cells- Solid pseudopapillary neoplasm (Giemsa 100x).



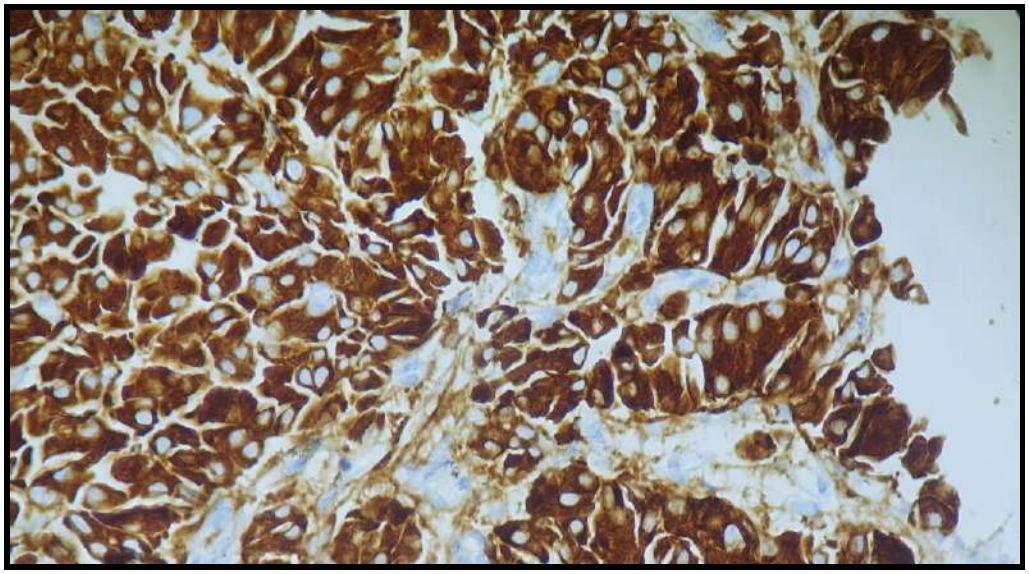
Picture 17- Category IV- Neoplastic

Photomicrograph shows a papillaroid cluster in which the cell lie away from fibrovascular core- Solid pseudopapillary neoplasm. (PAP 400x)

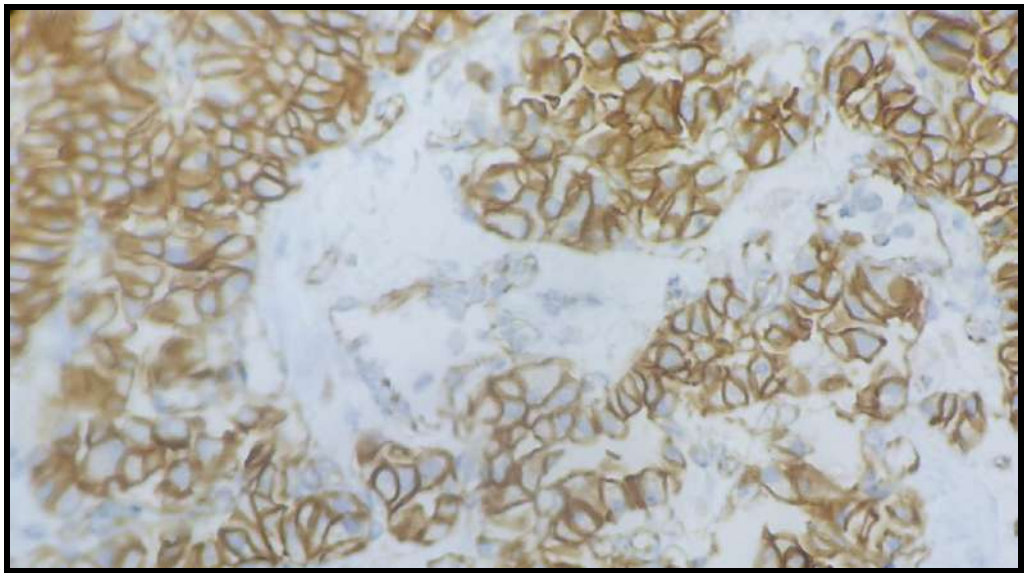


Picture 18- A case of Solid pseudopapillary neoplasm on cytology.

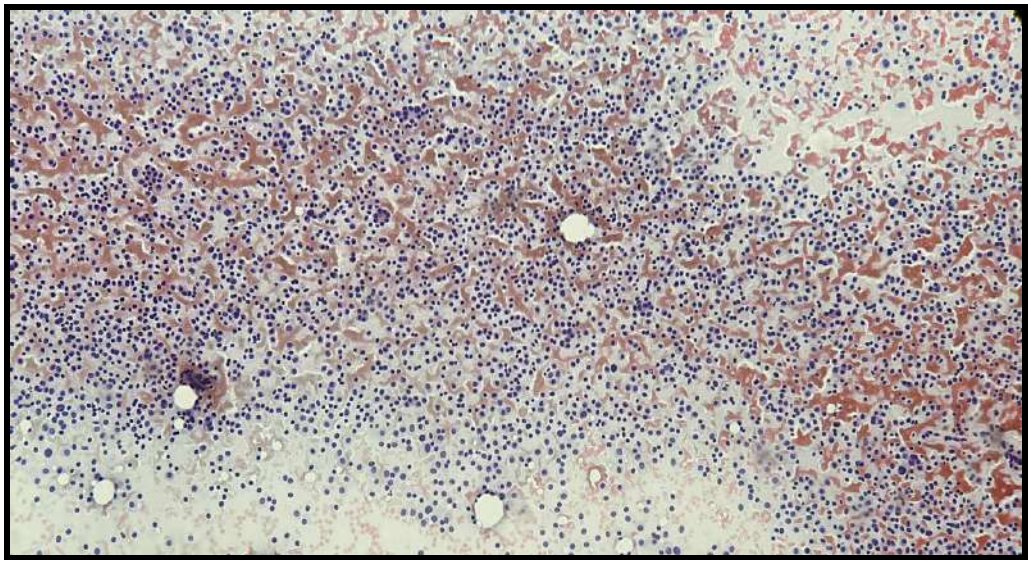
Photomicrograph show presence of tumor cells arranged in cords and nests having monomorphic nuclei with salt and pepper chromatin- Suggestive of pancreatic neuroendocrine tumor. (H&E 100x)



Picture 19- Photomicrograph shows strong cytoplasmic positivity of synaptophysin in a case of pancreatic neuroendocrine tumor (IHC 400x)

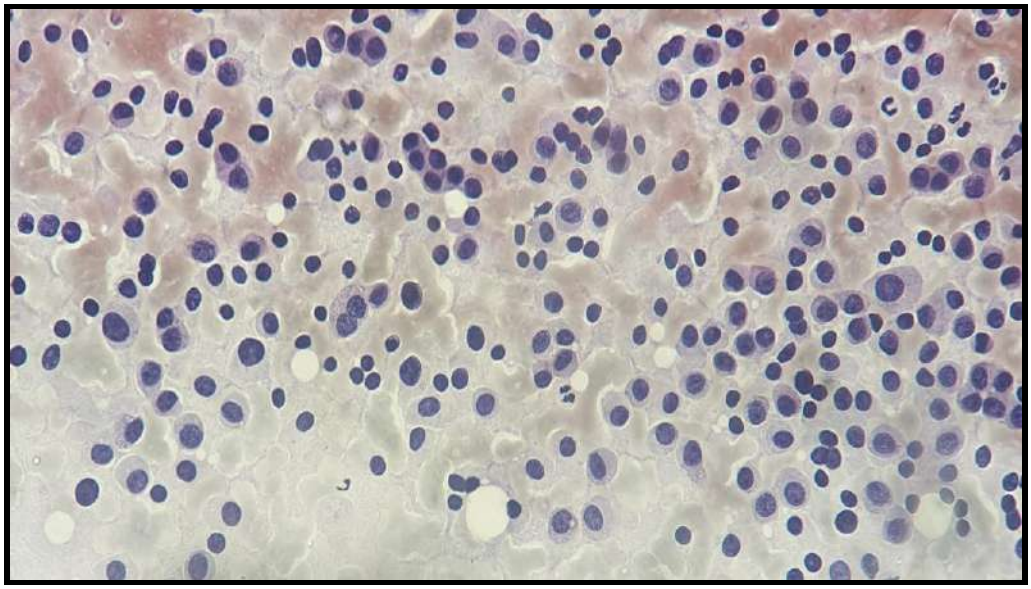


Picture 20- Photomicrograph shows negative nuclear staining of Beta-catenin in case of neuroendocrine tumor ruling out solid pseudopapillary neoplasm. (IHC 400x)



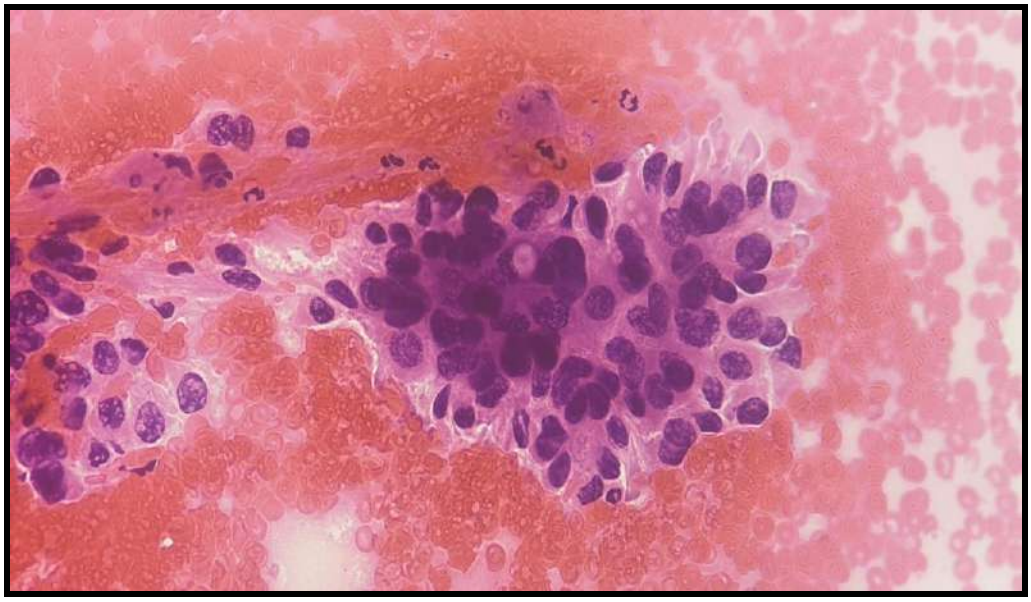
Picture 21- Category IV- Neuroendocrine tumor

Photomicrograph shows a moderately cellular smear exhibiting monotonous population of small to medium cells. (PAP 100x)



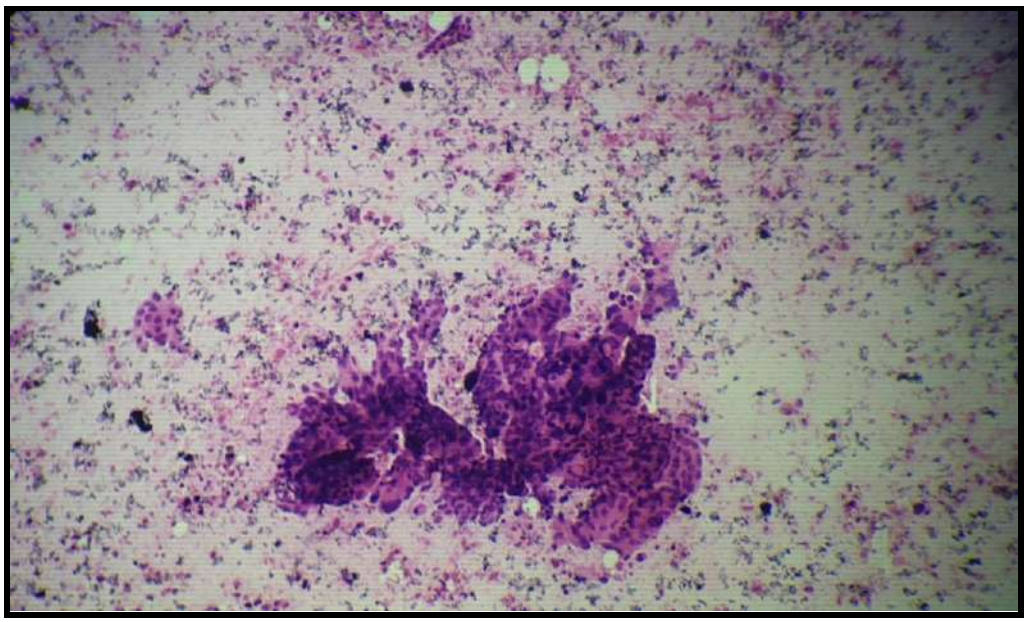
Picture 22- Category IV- Neoplastic, Neuroendocrine tumor

Photomicrograph shows small to medium sized cells having salt and pepper chromatin. (PAP 400x)



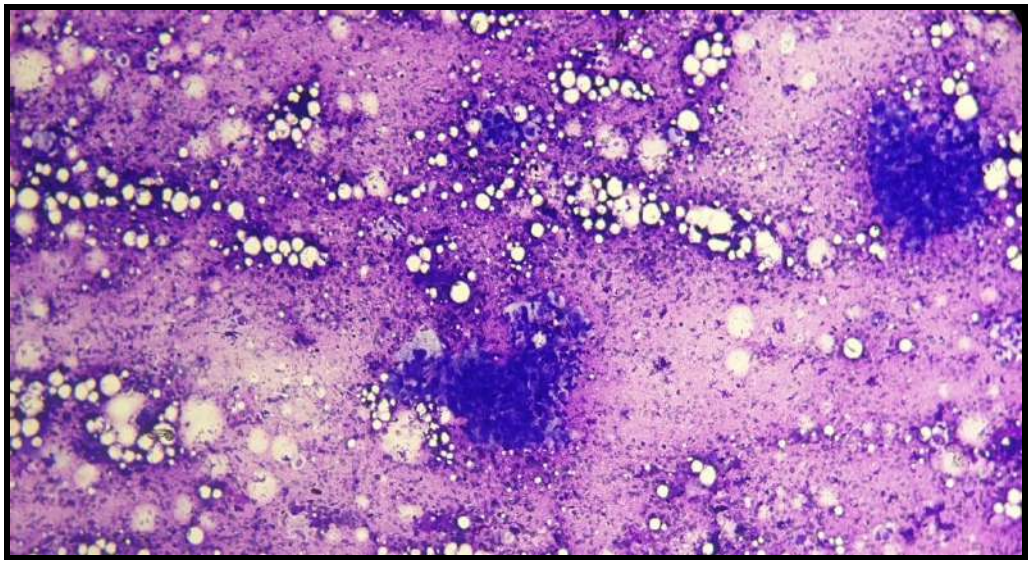
Picture 23- Category V- Suspicious

Photomicrograph shows papillaroid cluster of atypical cells exhibiting nuclear crowding and overlapping. There is mild to moderate degree of anisonucleosis. An occasional cell shows mucin filled intracytoplasmic vacuole (H&E 400x)



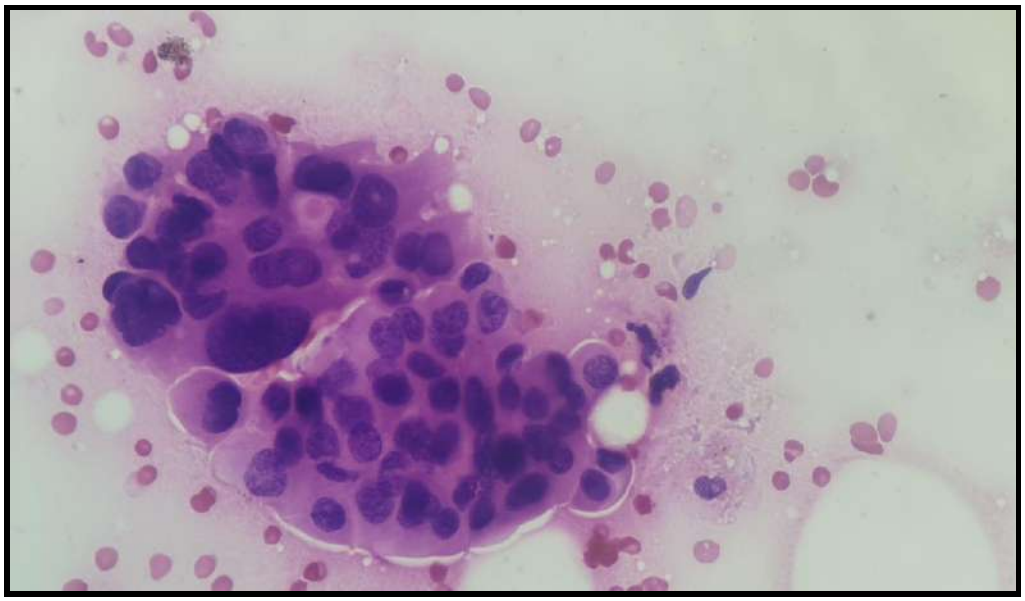
Picture 24 – Category VI- Positive or Malignant

Photomicrograph shows drunken honeycomb pattern of cells- Adenocarcinoma. (H&E 100x)



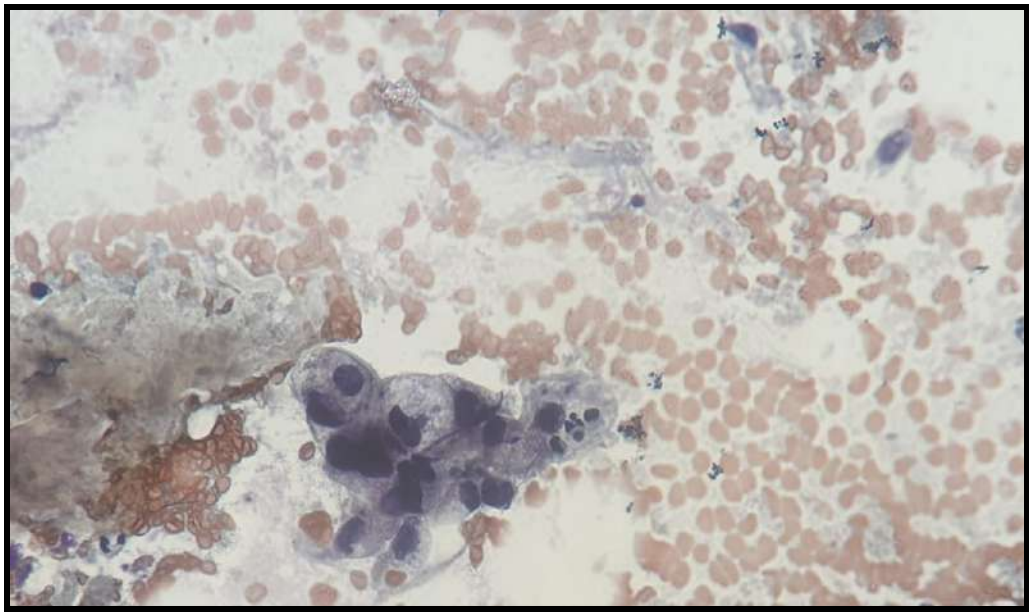
Picture 25- Category VI- Positive or Malignant

Low power view of Giemsa stain 100x shows cohesive clusters of atypical cells present against a necrotic background- Adenocarcinoma (Giemsa 100x)



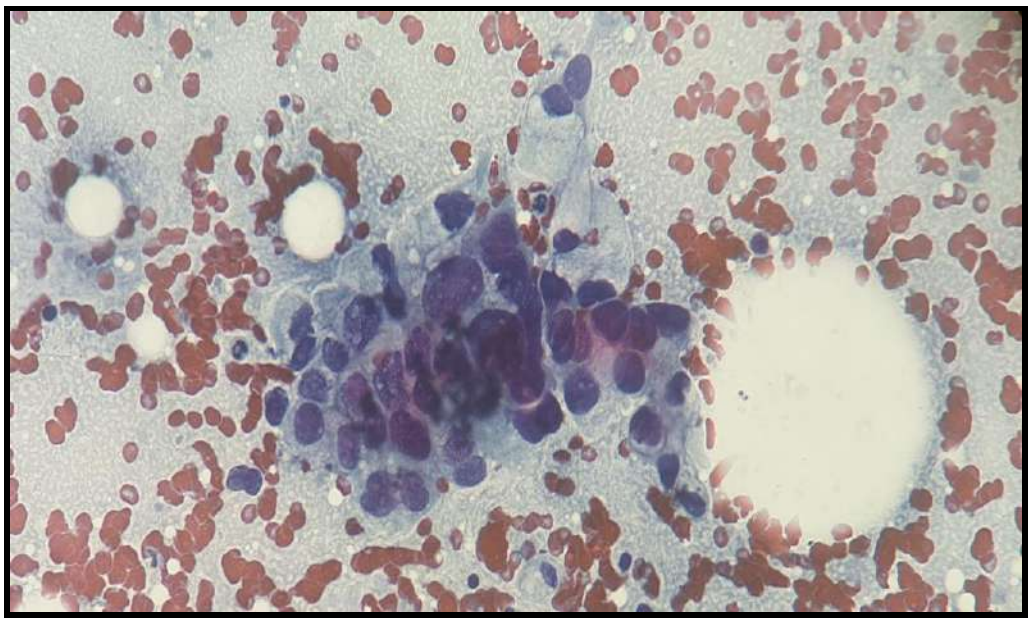
Picture 26- Category VI-Positive or Malignant

Photomicrograph show hard edged clusters of large atypical cells exhibiting moderate anisonucleosis (3:!) with nuclear overlapping and crowding-Adenocarcinoma (H&E 400x)



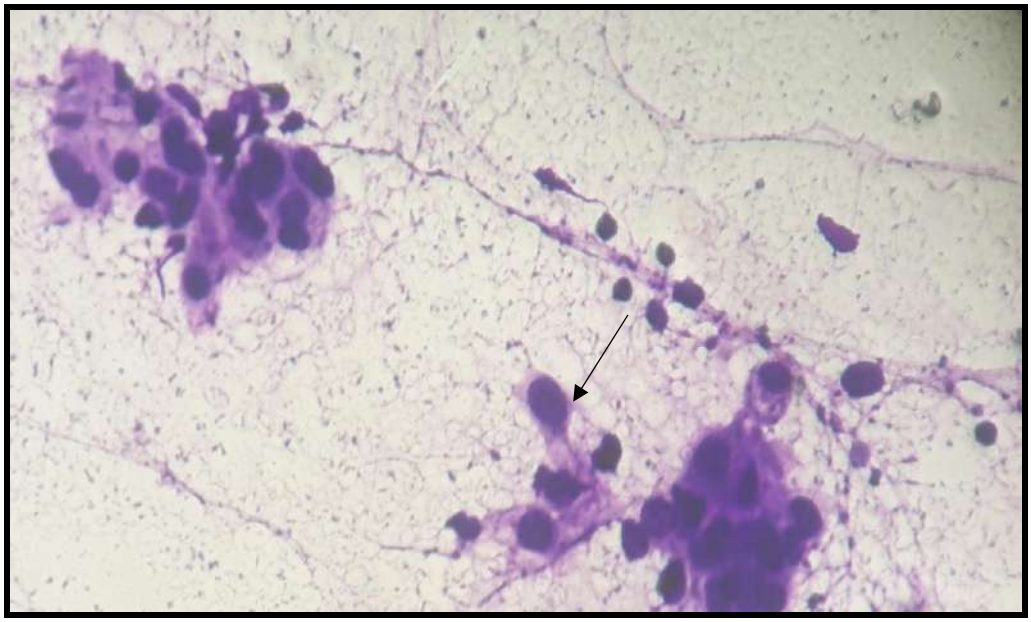
Picture 27- Category VI- Positive or Malignant

Photomicrograph show highly pleomorphic cells with presence of intracytoplasmic neutrophils- suggesting a high grade pathology- Adenocarcinoma. (PAP 400x)



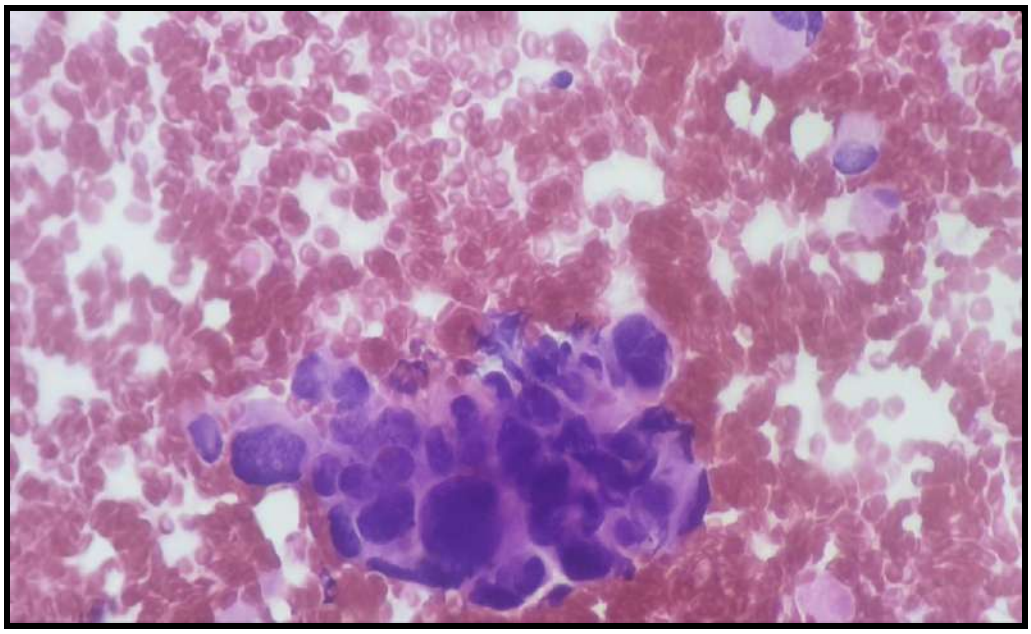
Picture 28- Category VI- Positive or Malignant

Photomicrograph show a cluster of cells having significant anisonucleosis (4:1) with prominent nucleoli- Adenocarcinoma (PAP 400x)



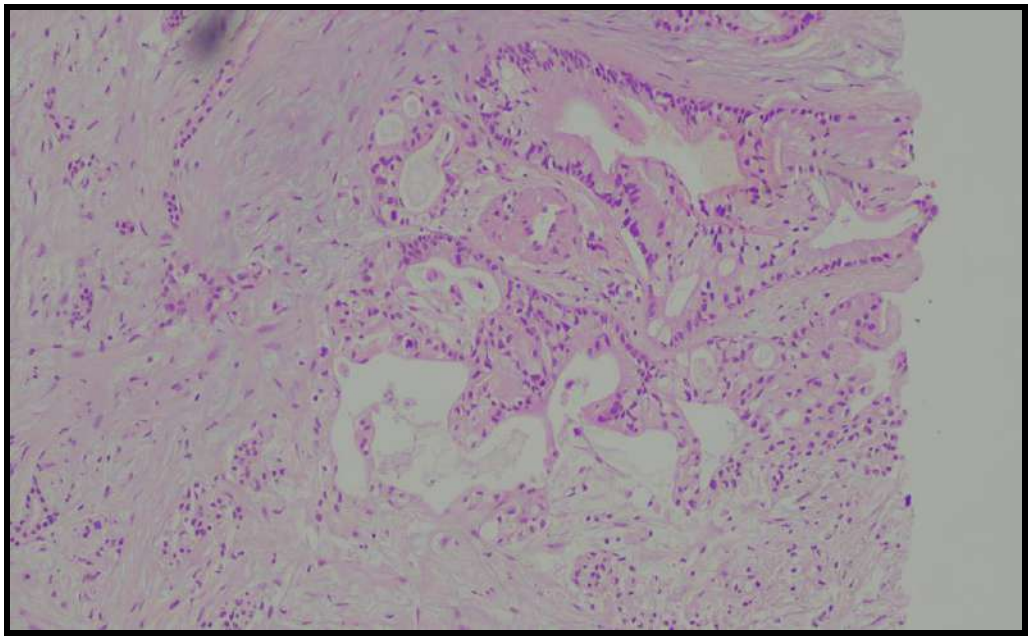
Picture 29-Category VI- Positive or Malignant

Photomicrograph show clusters of atypical cells with an occasional cell showing nuclear budding (arrow)-Adenocarcinoma (Giemsa 400x)

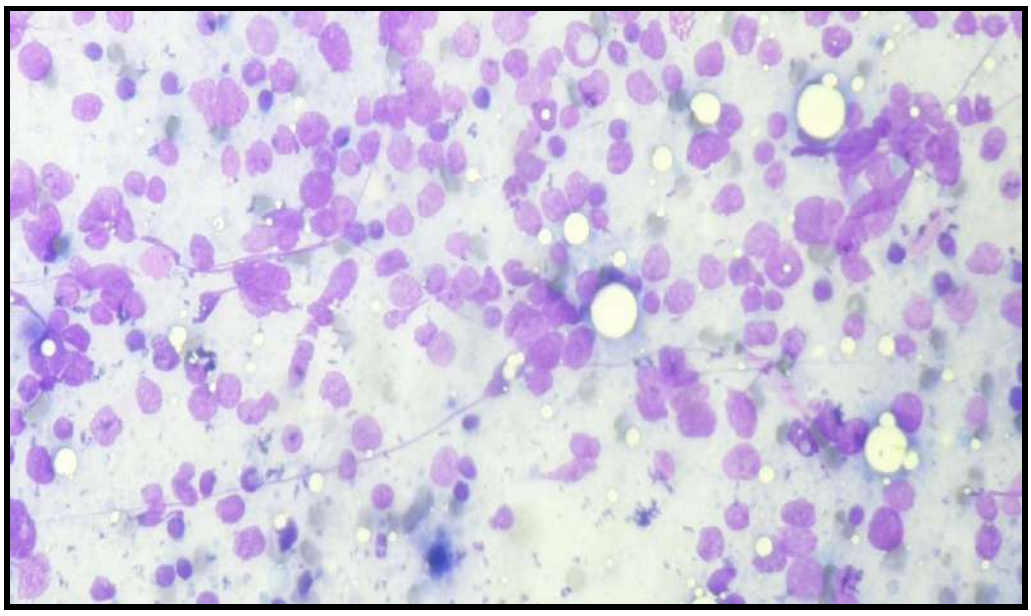


Picture 30 - Category VI- Positive or Malignant

Photomicrograph shows a cohesive cluster of atypical cells exhibiting marked anisonucleosis (4:1) with irregular nuclear contours - Adenocarcinoma (H&E 400x)

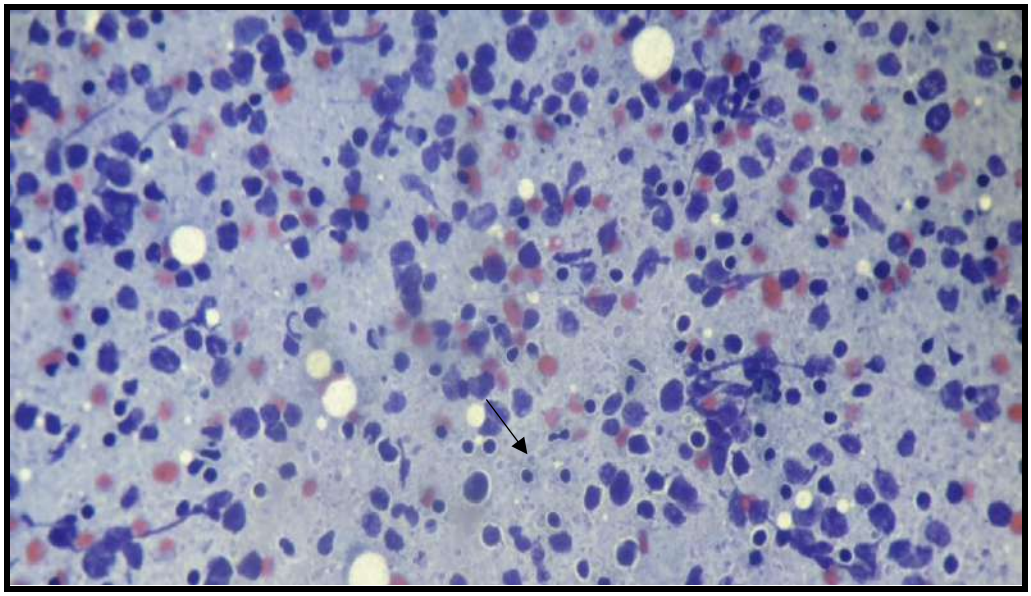


Picture 31- Photomicrograph of trucut biopsy pancreas shows presence of tumor arranged in glandular configuration with presence of extracellular mucin- Adenocarcinoma. (H&E 400x)



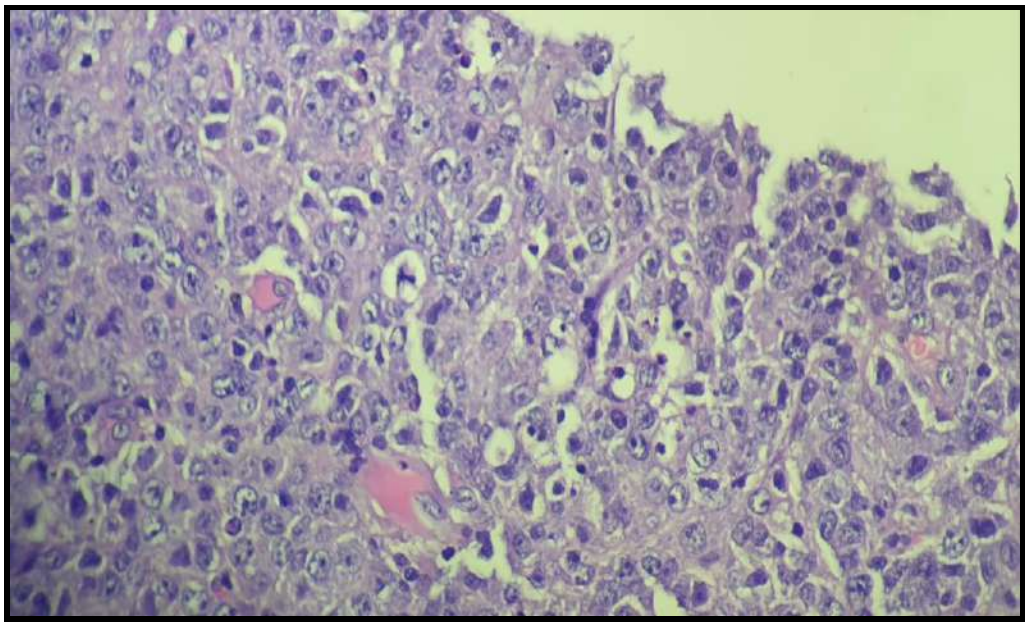
Picture 32- Category VI- Positive or Malignant

Photomicrograph show singly scattered medium sized atypical lymphoid cells having high N/C ratio, Fine chromatin and scant cytoplasm- Lymphoma (Giemsa 400x)



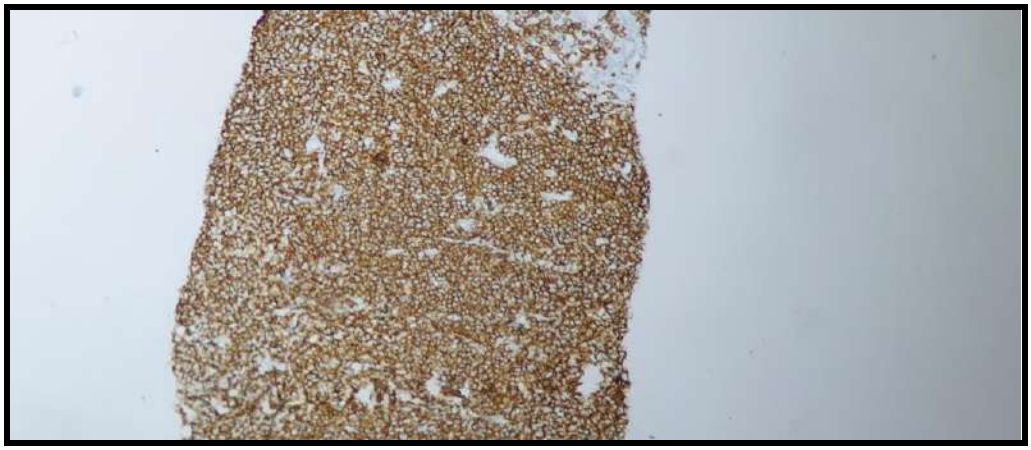
Picture 33- Category VI- Positive or Malignant

Photomicrograph shows atypical lymphoid cells with background showing lymphoglandular bodies (arrow)-Lymphoma (PAP 400x)



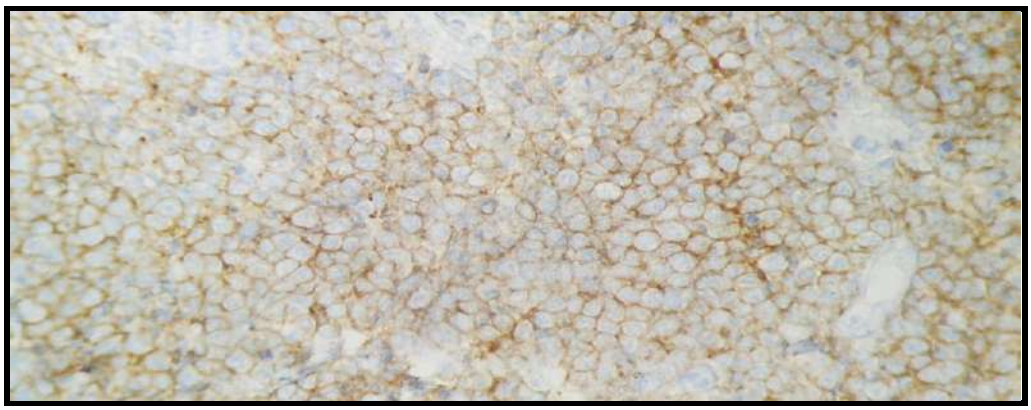
Picture 34–Burkitt's lymphoma

Photomicrograph shows presence of tumor cells in sheets having vesicular nuclei, fine nuclear chromatin and scant cytoplasm along with brisk atypical mitosis. (H&E 400x)



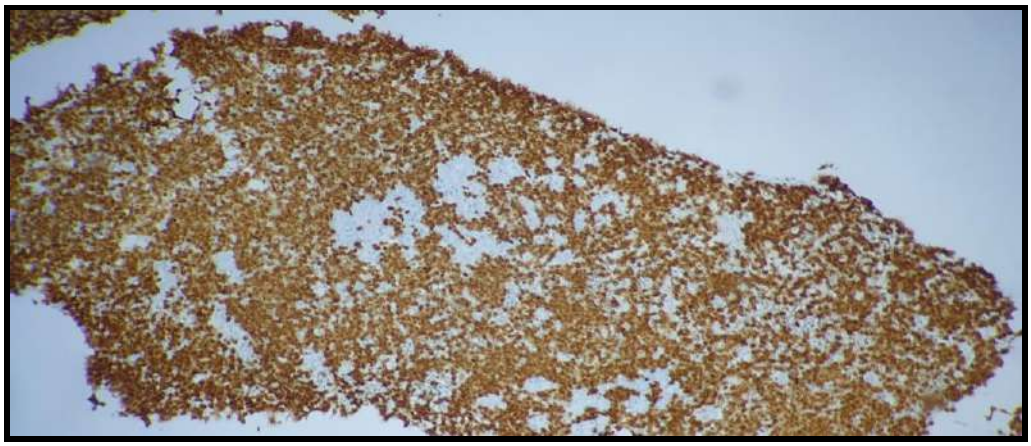
Picture 35- BCL6

Photomicrograph shows cytoplasmic positivity for BCL6- Burkitt's lymphoma (IHC 100x)



Picture 36-.c-myc

Photomicrograph shows cytoplasmic positivity of c-myc-Burkitt's lymphoma. (IHC 100x)



Picture 37- Mib1.

Mib1 is 98% in highest proliferating areas-Burkitt's lymphoma

(IHC 100x)

S. no	MRD number	Intials	Asp. Number	Age	Sex	Duration of symptoms	Symptoms					Past History	Personal History	Radiology	Biochemistry
							Vomiting and Nausea	Pain abdomen	Radiation of pain to back	Jaundice	Loss of weight and appetite				
1	866215	RP	2020-07	65	M	5 months	Absent	Present	Absent	Present	Present	DM+	Chronic Alchoholic	CECT abdomen-Markedly dilated pancreatic duct in body and tail region with abrupt cut off. Poorly marginated mass in body of pancreas infiltrating the soft tissue in retroperitoneal region- Malignancy	S.Calcium-9.7, S.Amylase-32, S.Lipase-9
2	876665	RD	2020-17	77	M	20 days	Absent	Present	Absent	Present	Present	DM+	-	MRCP- Poorly marginated and hypoenhancing mass lesion in relation to pancreatic head and adjoining uncinate process- Malignant	S.Calcium-10.0, ESR-28
3	306492	GK	2020-26	52	F	1 month	Absent	Present	Absent	Present	Absent	-	-	Endoscopic USG- Early chronic pancreatitis. Benign biliary stricture. Distal CBD stricture in periampullary location and mild biliary obstruction. No evidence of mass lesion elsewhere in pancreas or biliary region- Incomplete pancreatic divisum.	S.Calcium-9.3
4	870828	HS	2020-39	53	M	2 months	Present	Present	Present	Absent	Absent	DM+	Occasional Alchoholic	CECT- Ill defined enhancing retroperitoneal mass causing abrupt cuff off pancreatic duct and CBD. 3.5cm in diameter encasing superior mesentric artery with infiltration into duodenum and peritoneal deposits- Malignant	S.Calcium-9.3, TG-122 Amylase-75, Lipase-169
5	880520	SM	2020-52	55	M	15 days	Absent	Present	Absent	Present	Present	DM+	-	CT abdomen- Suggestive of multifocal autoimmune pancreatitis with distal CBD stricture and peripancreatic necrotic lymph node.	S.Calcium-9.0, S.Lipase- 304
6	882809	SS	2020-69	54	M	20 days	Absent	Present	Absent	Present	Present	-	Chronic Alchoholic, Chronic smoker	CT abdomen- Heterogenous soft tissue mass in relation to pancrease and peripancreatic lymphadenopathy with obstructive biliopathy.	S.Amylase-371, S.Lipase-12221
7	887685	JS	2020-114	50	M	6 months	Absent	Present	Absent	Absent	Present	DM+	Occasional Alchoholic	CECT abdomen- Ill defined mass in the pancreatic head and uncinate process with overdistention of CBD. Complete encasement of superior mesentric artery is seen- Pancreatic ductal adenocarcinoma	-
8	891246	RG	2020-148	59	F	3 months	Present	Present	Present	Present	Present	DM+,HTN+	-	-	-
9	825481	HS	2020-168	75	M	20 days	Present	Present	Absent	Present	Present	-	Occasional Alchoholic	MDCT abdomen- Carcinoma head of pancreas causing obstructive biliopathy with commen hepatic artery encasement and adherence of extrahepatic portal vein	-
10	887416	HS	2020-162	64	M	1 month	Absent	Present	Absent	Absent	Present	DM+	Chronic Alchoholic, Opioid addict	MRCP- Mass lesion in region of pancreatic body in background of chronic pancreatitis- Likely pancreatic adenocarcinoma	S.Calcium-10.8
11	907200	JR	2020-306	60	F	15 days	Present	Present	Present	Absent	Present	-	-	USG abdomen- Lesion in the distal body of pancreas and significant luminal narrowing	-
12	912303	JK	2020-345	50	F	15 days	Absent	Absent	Absent	Present	Absent	HTN+	-	USG abdomen- Pancreatic head mass with distal CBD and pancreatic duct obstruction	S.Calcium-9.2, ESR-16
13	894179	RK	2020-320	50	M	1 month	Present	Present	Present	Absent	Absent	-	-	-	S.Amylase-108, S.Lipase-38
14	892659	RM	2020-370	64	M	10 days	Absent	Present	Absent	Present	Present	DM+,HTN+	-	USG abdomen- Mass lesion in head of pancreas- suggestive of autoimmune pancreatitis	S.Calcium-9.2, ESR-30

S. no	MRD number	Blood findings	Tumor Markers	Mode of FNAC	Site	Cellularity	Architectural Pattern	Tumor cells	Granulomas	Necrosis	Inflammatory cells	Special Stains	Biopsy/Cell Block	IHC	Cytological Diagnosis
1	866215	TLC-7.1, Hb-10.9, Platelets-264	CA19.9-2022	USG guided	Body of pancreas	Adequate	Monolayered sheets and Clusters	Present	Absent	Absent	Foamy Macrophages	-	Ductal Adenocarcinoma-well differentiated	-	Atypical- Category III
2	876665	TLC-5.5, Hb-11.9, Platelets-221	CA19.9- 33510	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Present	Neutrophils, Foamy Macrophages, Giant cells	-	Ductal adenocarcinoma	-	Malignant aspirate-Adenocarcinoma-Category VI
3	306492	TLC-8.0, Hb-13.3, Platelets-237	CEA-2.96, CA19.9-73.2	Endoscopic guided	Body of pancreas	Adequate	Clusters of benign pancreatic acinar epithelial cells	Absent	Absent	Absent	Lymphocytes	-	-	-	Negative for malignancy- Category II
4	870828	TLC-5.4, Hb-11.0, Platelets-258	CA19.9- 123.6	Endoscopic guided	Head of pancreas	Adequate	Sheets and clusters	Present	Absent	Absent	Absent	-	-	-	Suspicious of malignancy- Category V
5	880520	TLC-6.5, Hb-9.6, Platelets- 323	CA19.9- 490, CEA-3.14	USG guided	Head of pancreas	Satisfactory	Clusters of large cells	Present	Absent	Absent	Absent	-	Ductal adenocarcinoma	-	Suspicious of malignancy- Category V
6	882809	TLC-6.5, Hb-9.6, Platelets- 323	CEA-7.82, CA19.9-86.2	USG guided	Head of pancreas	Adequate	-	Absent	Absent	Present	Lymphocytes	-	Fat necrosis	-	Negative for malignancy- Category-II
7	887685	TLC-6.5, Hb-9.6, Platelets- 330	CA19.9->500	Endoscopic guided	Head of pancreas	Adequate	Cohesive clusters	Present	Absent	Absent	Absent	-	-	-	Malignant aspirate- Adenocarcinoma-Category VI
8	891246	TLC-7.1, Hb-10.0, Platelets-189	-	Endoscopic guided	Head of pancreas	Adequate	Cohesive clusters	Present	Absent	Absent	Neutrophils	-	-	-	Malignant aspirate- Adenocarcinoma-Category VI
9	825481	TLC-9.0, Hb-9.2, Platelets- 230	-	Endoscopic guided	Head of pancreas	Inadeqaute	-	Absent	Absent	Absent	Foamy Macrophages	-	Carcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=focal+	Non Diagnostic-Category I
10	887416	TLC-8.5, Hb-12.6, Platelets-223	-	USG guided	Body of pancreas	Adequate	Cohesive clusters	Present	Absent	Absent	Absent	-	Ductal adenocarcinoma	-	Suspicious of malignancy- Category V
11	907200	TLC-8.5, Hb-10.9, Platelets-201	CA19.9- 703	Endoscopic guided	Body of pancreas	Adequate	Clusters of large cells	Present	Absent	Present	Lymphocytes	-	-	-	Atypical- Category III
12	912303	TLC-8.8, Hb-12.0, Platelets-251	-	USG guided	Head of pancreas	Adequate	Loosely cohesive clusters and few singly scattered	Present	Absent	Present	Absent	-	-	-	Malignant aspirate- Adenocarcinoma-Category VI
13	894179	TLC-12.3, Hb-10.6, Platelets-223	CA19.9- 17.3, CEA-3.11	Endoscopic guided	Head of pancreas	Adequate	Sheets of benign pancreatic acinar cells	Absent	Absent	Absent	Neutrophils and lymphocytes	-	-	-	Negative for malignancy- Category II
14	892659	TLC-12.5, Hb-9.6, Platelets-330	-	Endoscopic guided	Head of pancreas	Adequate	-	Absent	Absent	Absent	Lymphocytes	-	-	-	Negative for malignancy- Category II

S. no	MRD number	Intials	Asp. Number	Age	Sex	Duration of symptoms	Symptoms					Past History	Personal History	Radiology	Biochemistry
							Vomiting and Nausea	Pain abdomen	Radiation of pain to back	Jaundice	Loss of weight and appetite				
15	915583	SK	2020-388	55	M	1 month	Present	Present	Absent	Present	Absent	HTN+	Occasional Alchoholic	CT abdomen- Isoattentuating mass lesion in pancreatic head and uncinate process causing termination of CBD	S.Calcium-8.4
16	919948	CS	2020-424	60	M	15 days	Absent	Absent	Absent	Present	Absent	-	-	CECT abdomen- Pancreatic head and uncinate process mass causing obstructive biliopathy- ?pancreatic adenocarcinoma	S.Calcium-9.3, ESR-41
17	922328	SK	2020-444	60	M	3 months	Absent	Present	Absent	Absent	Absent	DM+	Chronic Alcoholic	CT abdomen-SOL in tail of pancreas with extensive hepatic and periportal metastasis with mild ascitis	S.Calcium-9.1, ESR-40
18	922404	MS	2020-447	74	M	3 months	Absent	Present	Present	Present	Present	DM+,HTN+	Chronic Alchoholic	MDCT- Advanced ductal adenocarcinoma with vascular encasement and periportal omental deposits	S.Calcium-10.8
19	923828	MM	2020-465	66	M	1 month	Absent	Present	Absent	Absent	Absent	DM+	-	PET scan- Pancreatic and liver lesion with abdominal lymphadenopathy	S.Calcium-8.6, ESR-18, S.Amylase-28, S.Lipase-31
20	928424	BS	2020-555	55	M	10 days	Absent	Present	Present	Absent	Present	-	-	CT abdomen- Ill defined heterogenous lesion arsing in relation to head and body of pancreas encasing celiac axis- neoplastic.	S.Calcium-8.7, ESR-18, S.Amylase-28, S.Lipase-31
21	594266	SS	2020-585	61	M	20 days	Present	Present	Absent	Absent	Present	DM+	Chronic Alchoholic, Chronic smoker	CT abdomen- Known case of chronic calcified pancreatitis. Large solid heterogenous mass in distal body and pancreatic tail with extension- Likely non functional neuroendocrine tumor	S.Calcium-8.2, S.Amylase-31, S.Lipase-10
22	85467	KS	2020-591	53	M	1 month	Present	Present	Absent	Absent	Absent	DM+	Chronic Alchoholic	-	S.Calcium-9.1
23	932553	GS	2020-653	65	M	1 month	Absent	Present	Absent	Absent	Present	DM+	Chronic Alchoholic	CT abdomen- Bulky and hypoechoic head and uncinate process lesion wirh dominant stricture in head of pancreas and collection in relation to pancreatic duct groove- chronic calcified pancreatitis.	S.Calcium-8.9, ESR-40
24	952175	PC	2020-847	10	F	10 days	Present	Present	Absent	Absent	Absent	-	-	USG abdomen- Pancreatic neck lesion with peripancreatic fat inflammation and collection noted	-
25	953095	KL	2020-856	56	M	1 month	Absent	Present	Present	Absent	Absent	-	-	CECT abdomen- Mass in pancreatic uncinate process with encasement of superior mesentric artery with narrowing of CBD, MPD and multiple hepatic and nodal metastasis	-
26	972321	GS	2020-970	60	M	1 month	Absent	Present	Present	Absent	Present	HTN+	-	USG abdomen- Peripancreatic mass causing obstructive biliopathy	S.Calcium-9.2, ESR-18
27	971378	VK	2020-984	70	M	1 month	Absent	Present	Absent	Absent	Absent	DM+	-	-	-
28	152393	JK	2020-1048	53	F	15 days	Absent	Present	Absent	Absent	Absent	-	-	CECT abdomen- Status partial pancreatectomy with few tiny hyperdense specks in relation to periphery of head of pancreas with well defined round thin walled cystic lesion in relation to superior aspect of head of pancreas.	-

S. no	MRD number	Blood findings	Tumor Markers	Mode of FNAC	Site	Cellularity	Architectural Pattern	Tumor cells	Granulomas	Necrosis	Inflammatory cells	Special Stains	Biopsy/Cell Block	IHC	Cytological Diagnosis
15	915583	TLC-6.4, Hb-11.2, Platelets-188	CA19.9-0.8, CEA-20.2	Endoscopic guided	Uncinate process of pancreas	Adequate	Clusters	Present	Absent	Absent	Absent	-	-	-	Suspicious of malignancy- Category V
16	919948	TLC-12.3, Hb-11.0, Platelets-233	-	USG guided	Head of pancreas	Adequate	Sheets, clusters and singly scattered	Present	Absent	Absent	Absent	-	Neuroendocrine tumor of pancreas	-	Neoplastic,Others-Category IV,Pancreatic solid pseudopapillary epithelial neoplasm
17	922328	TLC-8.6, Hb-11.3, Platelets-192	CA19.9-2290, CEA-6.57	USG guided	Tail of pancreas	Adequate	Clusters of atypical cells	present	Absent	Present	Absent	-	-	-	Malignant aspirate- Adenocarcinoma-Category VI
18	922404	TLC-11.5, Hb-12.9, Platelets-168	-	USG guided	Body of pancreas	Adequate	Papillaroid fragments and singly scattered	Present	Absent	Present	Neutrophils and lymphocytes	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=-, CDX2=-	Malignant aspirate- Adenocarcinoma-Category VI
19	923828	TLC-4.8, Hb-11.2, Platelets-230	CA19.9-1000	USG guided	Head of pancreas	Adequate	Loosely cohesive clusters and few singly scattered	Present	Absent	Present	Neutrophils, lymphocytes and foamy cells	-	Adenocarcinoma	Adenocarcinoma. CK7=+, CK20= Focal weak+, CEA=+, CDX2=Focal weak +, MiB1-15% in highest proliferating areas, Synaptophysin=-, Chromogranin=-	Malignant aspirate- Adenocarcinoma-Category VI
20	928424	TLC-9.7, Hb-13.9, Platelets-300	CA19.9-1000	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Adenocarcinoma	Adenocarcinoma. CK7=+, CEA=+, CK20=Focal+, CDX2=-, TTF1=-	Malignant aspirate- Adenocarcinoma-Category VI
21	594266	TLC-9.1 , Hb-8.0, Platelets-158	CA19.9-253, CEA-5.39	USG guided	Body of pancreas	Adequate	Papillaroid clusters	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Adenocarcinoma	Adenocarcinoma. CDX2=+, CK7=diffuse strong+, Chromogranin=-, Synaptophysin=-, CK2-=-, MiB1= 70% in highest proliferating areas	Atypical- Category III
22	85467	TLC-11.8, Hb-9.9, Platelets-185	-	Endoscopic guided	Head of pancreas	Adequate	Monolayered sheets, clusters and singly scattered ductal epithelial cells	Absent	Absent	Absent	Absent	-	-	-	Negative for malignancy- Category II
23	932553	TLC-13.8, Hb-14.9, Platelets-238	CA19.9-240	Endoscopic guided	Head of pancreas	Adequate	Sheets and clusters	Absent	Absent	Absent	Absent	-	-	-	Negative for malignancy- Category II
24	952175	TLC-14.7, Hb-12.9, Platelets-145	-	USG guided	Uncinate process of pancreas	Adequate	Singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Non Hodgkins lymphoma-B cell type (high grade), Favoring Burkitt's lymphoma	Non Hodgkins lymphoma-B cell type (high grade), Favoring Burkitt's lymphoma. LCA=+, CD20=+, CD10=+, Bcl6=+, MiB1= 98% in highest proliferating	Malignant round cell tumor, Possibly Lymphoma- Caetory VI
25	953095	TLC-9.7, Hb-11.9, Platelets-178	-	USG guided	Uncinate process of pancreas	Adequate	Papillaroid fragments, crowded and 3D clusters	Present	Absent	Absent	Foamy macrophages and Multinucleated giant cells	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20= weak+, CDX2=-	Malignant aspirate- Adenocarcinoma-Category VI
26	972321	TLC-12.6, Hb-9.9, Platelets-256	CA19.9-1136, CEA-57.5	USG guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	-	-	Malignant aspirate- Adenocarcinoma with mucinous differentiation- Category VI
27	971378	TLC-3.4, Hb-7.8, Platelets- 170	-	Endoscopic guided	Head of pancreas	Adequate	Few cohesive clusters	Present	Absent	Absent	Lymphocytes	-	-	-	Neoplastic- Others. Mucinous cystic lesion with low grade atypia. Category-IV
28	152393	TLC-4.3, Hb-11.2, Platelets-200	-	Endoscopic guided	Head of pancreas	Adequate	Clusters of benign pancreatic acinar epithelial cells	Absent	Absent	Absent	Foamy Macrophages	-	-	-	Negative for malignancy, Category II-Benign cystic lesion

S. no	MRD number	Intials	Asp. Number	Age	Sex	Duration of symptoms	Symptoms					Past History	Personal History	Radiology	Biochemistry
							Vomiting and Nausea	Pain abdomen	Radiation of pain to back	Jaundice	Loss of weight and appetite				
29	982930	PS	2020-1072	88	M	1 month	Present	Present	Present	Present	Present	DM+,HTN+	-	CECT abdomen- Carcinoma head of pancreas with obstruction of CBD, MPD and few locoregional lymph nodes metastasis	-
30	992041	GS	2020-1193	71	M	10 days	Absent	Present	Absent	Absent	Absent	-	Chronic Alchoholic	CECT abdomen- Findings are suggestive of pancreatic ductal adenocarcinoma involving head of pancreas with abuttment of superior mesentric artery.	-
31	1001190	MK	2020-1232	25	F	1 month	Absent	Present	Absent	Absent	Absent	-	-	MRI abdomen- Exophytic mass arising from neck of pancreas extending into porta-hepatis- concerning of pancreatic neoplasm	-
32	1008021	TL	2021-23	45	M	2 months	Absent	Present	Present	Absent	Present	HTN+	Chronic Alchoholic, Chronic smoker	-	S.Calcium-8.7, ESR-84, S.Amylase-719, S.Lipase-672, TG-61.0
33	1009834	KK	2021-28	50	F	3 months	Absent	Present	Absent	Absent	Absent	-	-	CT scan- Ill defined hypodense lesion in relation to the body of the pancreas leading to upstream dilation of MPD with congestion of retropancreatic fascia adjacent to lesion and enlarged lymph nodes in para-aortic area.	-
34	1018899	SS	2021-137	58	M	3 months	Present	Present	Present	Absent	Present	DM+,HTN+	Chronic Alchoholic	CT scan- Findings are suugestive of acute necrotizing pancreatitis and acute necrotic collection in pancreatic body and tail involving full thickness of pancreatic parenchyma. Duct discontinuation not ruled out. Splenic vein thrombosis seen.	S.Calcium-9.1, ESR- 18, TG-110, Cholestrol-161, S.Amylase-78, S.Lipase- 21
35	1097803	ML	2021-531	58	F	20 days	Present	Present	Absent	Absent	Absent	-	-	-	S.Calcium- 7.9
36	1093325	SS	2021-540	67	M	15 days	Present	Present	Present	Present	Present	-	Chronic Alchoholic	-	S.Calcium-7.3, S.Amylase-57, S.Lipase-10
37	1096512	RK	2021-549	58	M	1 month	Absent	Present	Absent	Absent	Absent	-	Chronic Alchoholic, Chronic smoker	-	-
38	1096896	SS	2021-551	50	M	20 days	Present	Present	Absent	Absent	Present	-	Chronic Alchoholic	CT scan- Ill defined hypermetabolic soft tissue mass lesion arising from head, neck and body of pancreas- primary malignancy	-
39	1099974	SJ	2021-554	59	F	2 months	Present	Present	Present	Absent	Present	DM+,HTN+	-	-	-
40	1083389	BS	2021-609	50	M	2 months	Absent	Present	Absent	Absent	Present	-	Chronic Alchoholic, Chronic smoker	-	S.Calcium-9.0
41	1115155	ML	2021-649	75	M	10 days	Absent	Present	Absent	Absent	Absent	DM+	Chronic Alchoholic, Chronic smoker	USG abdomen- Obscured by gas shadow. Bilateral gradel renal parenchymal changes with over distended gall bladder.	S.Calcium-9.7
42	1118596	KK	2021-675	76	F	1 month	Absent	Present	Absent	Present	Present	DM+	-	-	S.Calcium-8.3

S. no	MRD number	Blood findings	Tumor Markers	Mode of FNAC	Site	Cellularity	Architectural Pattern	Tumor cells	Granulomas	Necrosis	Inflammatory cells	Special Stains	Biopsy/Cell Block	IHC	Cytological Diagnosis
29	982930	TLC-5.3, Hb-12.3, Platelets-148	-	USG guided	Head of pancreas	Adequate	Loosely cohesive clusters and few singly scattered	Present	Absent	Absent	Neutrophils and lymphocytes	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20= weak+, CDX2=weak+	Malignant aspirate- Adenocarcinoma-Category VI
30	992041	TLC-11.5, Hb-12.9, Platelets-168	CA19.9->500	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Absent	-	Adenocarcinoma	Adenocarcinoma. CK7=+, CEA=+, CK20=-, CDX2=focal+, TTF1=-	Malignant aspirate- Adenocarcinoma-Category VI
31	1001190	TLC-8.5, Hb-12.6, Platelets-223	-	USG guided	Uncinate process of pancreas	Adequate	Epithelioid cell granuloma	Absent	Present	Present	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	20% ZN- Non contributary	-	-	Negative for malignancy- Category II. Granulomatous Inflammation
32	1008021	TLC-7.2, Hb-10.2, Platelets-243	CEA-2.62	Endoscopic guided	Head of pancreas	Adequate	Sheets of ductal epithelial cells	Absent	Absent	Present	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	-	-	Negative for malignancy- Category II, Pseudocyst
33	1009834	TLC-8.0, Hb-12.5, Platelets-228	-	Endoscopic guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Absent	-	Ductal adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
34	1018899	TLC-5.5, Hb-12.2, Platelets-102	CA19.9-49.8, CEA-20.18	USG guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Present	Absent	-	Ductal adenocarcinoma	Adenocarcinoma. CK7=+, CEA=+, CK20=Focal+, CDX2=-	Malignant aspirate- Adenocarcinoma-Category VI
35	1097803	TLC-5.3, Hb-12.3, Platelets-148	-	USG guided	Head of pancreas	Adequate	Papillaroid clusters, tissue fragments and cohesive clusters	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Ductal adenocarcinoma	-	Suspicious of malignancy- Category V
36	1093325	TLC-6.1, Hb-13.8, Platelets-218	CA19.9-206.6, CEA-1.89	USG guided	Tail of pancreas	Adequate	Loosely cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Foamy macrophages and Multinucleated giant cells	-	Inadequate for opinion-Non diagnostic	-	Malignant aspirate-Mucin secreating Adenocarcinoma- Category VI
37	1096512	TLC-10.4, Hb-15.9, Platelets-330	CA19.9-9900, CEA-69	USG guided	Head of pancreas	Adequate	Tiny clusters and singly scattered	Present	Absent	Present	Neutrophils and foamy macrophages	-	Ductal adenocarcinoma	Ductal Adenocarcinoma. CK7=+, CEA=focal+, CK20=hetrogenous+, CDX2=focal+	Suspicious of malignancy- Category V
38	1096896	TLC-7.0, Hb-13.2, Platelets-184	CA19.9- 1120.6	USG guided	Head of pancreas	Adequate	Cohesive clusters and some papillaroid fragments	Present	Absent	Present	Neutrophils, lymphocytes and foamy cells	-	Ductal adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
39	1099974	TLC-10.9, Hb-13.8, Platelets-98	CA19.9-2486, CEA-7.2	USG guided	Head of pancreas	Adequate	Cohesive and dyscohesive clusters with papillaroid fragments	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=diffuse+, CEA=+, CK20= heterogenous+, CDX2=focal+	Malignant aspirate- Adenocarcinoma-Category VI
40	1083389	TLC-11.6, Hb-12.2, Platelets-270	CA19.9-0.8, CEA-2.74	USG guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Present	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=-, CK20=+	Malignant aspirate- Adenocarcinoma-Category VI
41	1115155	TLC-7.9, Hb-10.9, Platelets-136	CA19.9-1895, CEA-32.8	USG guided	Head of pancreas	Adequate	Cohesive clusters	Present	Absent	Absent	Neutrophils	-	-	-	Malignant aspirate- Adenocarcinoma-Category VI
42	1118596	TLC-6.4, Hb-10.6, Platelets-144	CA19.9-1895, CEA-5.6	USG guided	Head of pancreas	Adequate	Few clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Inadequate for opinion- non diagnostic	-	Malignant aspirate- Adenocarcinoma-Category VI

S. no	MRD number	Intials	Asp. Number	Age	Sex	Duration of symptoms	Symptoms					Past History	Personal History	Radiology	Biochemistry
							Vomiting and Nausea	Pain abdomen	Radiation of pain to back	Jaundice	Loss of weight and appetite				
43	1113361	BS	2021-680	63	M	4 months	Present	Present	Present	Absent	Present	-	Chronic Alchoholic	-	-
44	1126624	MS	2021-732	56	M	6 months	Absent	Present	Present	Present	Present	DM+	Chronic Alchoholic	-	S.Calcium-9.7, S.Amylase-100, S.Lipase- 134
45	1127695	VR	2021-735	44	M	2 months	Present	Present	Present	Absent	Present	DM+,HTN+	Chronic Alchoholic	-	-
46	1125574	SK	2021-742	55	F	2 months	Absent	Present	Absent	Absent	Absent	-	-	CECT abdomen- Hypoenhancing mass measuring 2.5x1.6cm in the head of pancreas- likely malignant	-
47	1126838	IS	2021-747	66	F	20 days	Absent	Present	Absent	Absent	Present	-	-	CECT abdomen- Findings are suggestive of adenocarcinoma head and uncinate process of pancreas with abrupt cut off main pancreatic duct and upstream pancreatic parenchymal atrophy.	S.Amylase-103, S.Lipase-106
48	1132710	GS	2021-927	52	M	1 month	Absent	Present	Absent	Absent	Absent	-	-	-	
49	1145679	SS	2021-928	65	M	1 month	Absent	Present	Absent	Absent	Absent	DM+	Chronic Alchoholic	-	S.Calcium-10.0, S.Amylase-92, S.Lipase- 126
50	1154809	BKK	2021-1030	78	M	15 days	Present	Present	Present	Absent	Present	DM+,HTN+	-	CECT abdomen- Long loculated collection in hepatoduodenal ligament with small collection in the region of distal body and tail- Likely secondary to pancreatitis	S.Calcium-9.1, S.Amylase-116, S.Lipase-150
51	1165196	SK	2021-1117	60	M	1 month	Present	Present	Absent	Absent	Present	DM+	Occasional Alchoholic	CECT abdomen- Exophytically buldging necrotic mass lesion involving pancreatic head causing abrupt change in the calibre of MPD and upstream pancreatic parenchymal atrophy with vascular encasement.	S.Calcium-9.5, S.Amylase-21, S.Lipase-10
52	1175311	PC	2021-1213	47	M	2 years	Absent	Present	Absent	Absent	Absent	-	-	USG abdomen- Well circumscribed hypoechoic solid mass in the proximal body of pancreas- Likely neoplastic	S.Amylase-179, S.Lipase-288
53	1197481	SS	21-1409	55	M	20 days	Absent	Present	Absent	Absent	Absent	-	-	CECT abdomen- Hypodense lesion in the head and uncinate process of pancreas ?malignant ?nature with multiple hepatic lesions ?metastasis	-
54	1196281	SS	21-1412	75	M	15 days	Present	Present	Absent	Present	Absent	DM+	-	MDCT- Malignancy involving head of pancreas with obstructive biliopathy and dilated pancreatic duct.	ESR-85, S.Lipase-4
55	1191905	SK	21-1418	65	F	2 months	Absent	Present	Absent	Absent	Present	HTN+	-	CT scan abdomen- Suggestive of advanced pancreatic duct adenocarcinoma with vascular encasement. Right adenxal malignancy.	-
56	1208789	BK	21-1502	55	F	3 months	Present	Present	Present	Absent	Absent	-	-	CECT abdomen- Ill defined heterogenous soft tissue lesion in the body of pancreas with extent and atrophic distal body and tail of pancreas- likely adenocarcinoma.	-

S. no	MRD number	Blood findings	Tumor Markers	Mode of FNAC	Site	Cellularity	Architectural Pattern	Tumor cells	Granulomas	Necrosis	Inflammatory cells	Special Stains	Biopsy/Cell Block	IHC	Cytological Diagnosis
43	1113361	TLC-10.3, Hb-9.9, Platelets-136	CA19.9-0.8, CEA-165	USG guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Present	Neutrophils and lymphocytes	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=-, CK20=+	Malignant aspirate- Adenocarcinoma-Category VI
44	1126624	TLC-7.0, Hb-11.5, Platelets-184	CA19.9-273.3, CEA-70.8	USG guided	Body of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Chronic pancreatitis	-	Malignant aspirate- Adenocarcinoma-Category VI
45	1127695	TLC-8.3, Hb-10.0, Platelets-235	CA19.9-3.2, CEA-1.55	USG guided	Body of pancreas	Adequate	Epithelioid cell granuloma	Absent	Present	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	20% ZN- Non contributary, GMS-Negative, PAS-Negative	Inadequate for opinion	-	Negative for malignancy- Category II. Granulomatous Inflammation
46	1125574	TLC-8.7, Hb-13.6, Platelets-349	CA19.9-0.8	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=weak+, CDX2=-	Malignant aspirate- Adenocarcinoma-Category VI
47	1126838	TLC-8.3, Hb-12.3, Platelets-271	CA19.9-44.0, CEA-0.5	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Chronic pancreatitis	-	Malignant aspirate- Adenocarcinoma-Category VI
48	1132710	TLC-9.7, Hb-13.9, Platelets-300	CA19.9-1654	USG guided	Tail of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Inadequate for opinion- non diagnostic	-	Malignant aspirate- Adenocarcinoma-Category VI
49	1145679	TLC-15.6, Hb-15.0, Platelets-187	CA19.9-293, CEA-6.47	USG guided	Uncinate process of pancreas	Adequate	Papillaroid clusters, tissue fragments and cohesive clusters	Present	Absent	Present	Neutrophils and foamy macrophages	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=-, CDX2=-	Malignant aspirate- Adenocarcinoma-Category VI
50	1154809	TLC-9.7, Hb-13.9, Platelets-300	CA19.9-14.2, CEA-0.45	USG guided	Tail of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils	-	Chronic pancreatitis	-	Neuroendocrine tumor-Neoplastic-Category IV
51	1165196	TLC-12.4, Hb-10.8, Platelets-185	-	USG guided	Head of pancreas	Partly degenerated smears	3D Clusters	Present	Absent	Present	Neutrophils, Foamy Macrophages, Giant cells	-	Non diagnostic	-	Suspicious of malignancy- Category V
52	1175311	TLC-14.4, Hb-11.9, Platelets-300	CA19.9-13.7, CEA-288	USG guided	Body of pancreas	Adequate	3D clusters and papillaroid fragments	Present	Absent	Absent	Absent	-	Ductal adenocarcinoma-Moderat;y differentiated	-	Suspicious of malignancy- Category V
53	1197481	TLC-8.6, Hb-11.3, Platelets-192	CA19.9-97.81	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Absent	-	Inadequate-Non diagnostic	-	Malignant aspirate- Adenocarcinoma-Category VI
54	1196281	TLC-6.7, Hb-9.9, Platelets- 118	CA19.9-1982, CEA-24.23	USG guided	Head of pancreas	Scantly cellular	few cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, Foamy Macrophages, Giant cells	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=-	Suspicious of malignancy- Category V
55	1191905	TLC-9.7, Hb-11.9, Platelets-178	CA19.9-0.8, CEA-6.91	USG guided	Head of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
56	1208789	TLC-6.4, Hb-10.6, Platelets-144	-	USG guided	Body of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI

S. no	MRD number	Intials	Asp. Number	Age	Sex	Duration of symptoms	Symptoms					Past History	Personal History	Radiology	Biochemistry
							Vomiting and Nausea	Pain abdomen	Radiation of pain to back	Jaundice	Loss of weight and appetite				
57	1210711	BL	21-1515	77	F	1 month	Absent	Present	Absent	Absent	Absent	DM+	-	CECT abdomen- Heterogeneously enhancing ill defined soft tissue density mass lesion in body and tail of pancreas with poor fat planes encasing celiac artery, splenic vessels. Areas of necrosis and internal vascularity seen- Primary mitotic pathology.	-
58	1213130	MK	21-1542	68	F	20 days	Absent	Present	Absent	Present	Absent	-	-	CECT abdomen- Imaging shows 3.7x2.7cm infiltrating growth (malignant) in relation to distal most CBD/Periampullary location with its visceral and vascular relations as described.	-
59	1212662	JS	21-1546	78	M	1 year	Present	Present	Absent	Present	Present	-	Occasional Alchoholic	MRCP- Pancreatic head malignancy with vascular involvement, biliary obstruction and lymph node and peritoneal disease as described.	S.Calcium- 8.7
60	1209355	MS	21-1568	56	M	1 month	Absent	Present	Absent	Absent	Absent	DM+	Chronic Alchoholic	-	S.Amylase- 71.0, S.Lipase- 24
61	1219143	NK	21-1605	56	F	2 months	Absent	Present	Present	Present	Present	-	-	PET CT- FDG avid mass lesion in the head region of pancreas with extent and involvement- Malignant primary disease.	S.Calcium-9.7, S.Amylase- 88.0, S.Lipase-75
62	1225830	KS	21-1658	51	M	2 months	Present	Present	Absent	Present	Absent	-	Chronic Alchoholic	CT scan abdomen- Extrahepatic biliary obstruction resulting from encasement anf occulsion of CBD by mass lesion arising in relation to head of pancreas- Double duct sign seen.	-
63	1225168	BS	21-1683	68	M	3 months	Absent	Present	Absent	Absent	Present	-	Chronic Alchoholic	CECT abdomen- Findings are suggestive of advanced pancreatic malignancy with hepatic metastasis.	-
64	1230850	MB	21-1697	63	F	2 months	Absent	Present	Present	Absent	Present	DM+,HTN+	-	CT scan abdomen- 5 cmm lesion in pancreatic body and tail closely abutting hepatic and splenic artery.	-
65	1239126	HR	22-56	67	M	20 days	Absent	Present	Absent	Present	Present	DM+,HTN+	Chronic Alchoholic	CT abdomen- Complex heterogeneously enhancing mass involving the head and body of pancreas infiltrating in to CBD and superior mesentric vein likely primary- Pancreatic malignancy.	-
66	1133649	MS	22-76	57	M	2 months	Absent	Present	Present	Present	Present	-	Chronic Alchoholic	USG abdomen- In a known case of pancreatitis, organised collection of small liquified component noted.	S.Calcium-9.7
67	1128762	GS	22-103	62	M	1 month	Absent	Present	Present	Absent	Present	DM+,HTN+	Chronic Alchoholic	CT abdomen- Complex heterogeneously enhancing mass involving the head and body of pancreas infiltrating in to CBD and superior mesentric vein likely primary- Pancreatic malignancy.	-
68	1258114	KK	22-240	77	F	2 months	Absent	Present	Present	Present	Present	-	-	USG abdomen- Hypoechoic lesion in pancreatic head	-
69	1261249	KP	22-336	53	M	3 months	Absent	Present	Absent	Absent	Present	DM+	-	CT abdomen- Cystic lesion in uncinate process communicating with main pancreatic duct and accesory duct- Likely side branch intraductal pancreatic mucinous neoplasm.	S.Calcium-9.7
70	1276461	SS	22-418	85	M	2 months	Absent	Present	Absent	Absent	Absent	DM+	-	MRCP- Ill defined hypoenhancing mass lesion involving head and uncinate process with double duct sign and obstructive biliopathy with encasement of superior mesentric artery- Advanced pancreatic malignancy.	-

S. no	MRD number	Blood findings	Tumor Markers	Mode of FNAC	Site	Cellularity	Architectural Pattern	Tumor cells	Granulomas	Necrosis	Inflammatory cells	Special Stains	Biopsy/Cell Block	IHC	Cytological Diagnosis
57	1210711	TLC-5.5, Hb-11.9, Platelets-221	CA19.9-70.56, CEA-119.6	USG guided	Body of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
58	1213130	TLC-6.5, Hb-11.4, Platelets-264	-	USG guided	Head of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
59	1212662	TLC-7.0, Hb-13.2, Platelets-184	CA19.9-1982, CEA-19.65	USG guided	Head of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes, multinucleated giant cells and foamy cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
60	1209355	TLC-13.8, Hb-14.9, Platelets-238	CA19.9-1892	USG guided	Tail of pancreas	Satisfactory	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Present	Neutrophils, Foamy Macrophages, Giant cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
61	1219143	TLC-12.4, Hb-10.8, Platelets-185	-	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Ductal adenocarcinoma	-	Suspicious of malignancy- Category V
62	1225830	TLC-4.3, Hb-11.2, Platelets-200	-	USG guided	Head of pancreas	Adequate	Cohesive clusters and some papillaroid fragments	Present	Absent	Absent	Neutrophils	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
63	1225168	TLC-14.4, Hb-11.9, Platelets-300	CA19.9-145, CEA-3	USG guided	Head of pancreas	Adequate	Cohesive clusters and some papillaroid fragments	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Ductal adenocarcinoma	Ductal adenocarcinoma. CK7=+, CEA=+, CK20=heterogenous+, CDX2=+	Malignant aspirate- Adenocarcinoma-Category VI
64	1230850	TLC-5.4, Hb-11.0, Platelets-258	-	USG guided	Body of pancreas	Scantly cellular	Cohesive clusters and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
65	1239126	TLC-11.5, Hb-12.9, Platelets-168	CA19.9-1211	USG guided	Head of pancreas	Adequate	Cohesive clusters, papillaroid fragments and singly scattered	Present	Absent	Absent	Neutrophils, lymphocytes and foamy cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
66	1133649	TLC-15.6, Hb-15.0, Platelets-187	-	USG guided	Body of pancreas	Adequate	Cohesive clusters and some papillaroid fragments	Present	Absent	Absent	Multinucleated cells	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
67	1128762	TLC-6.4, Hb-10.6, Platelets-144	CA19.9-1022	USG guided	Head of pancreas	Adequate	Cohesive and dyscohesive clusters with papillaroid fragments	Present	Absent	Absent	Neutrophils and foamy macrophages	-	Adenocarcinoma	-	Malignant aspirate- Adenocarcinoma-Category VI
68	1258114	TLC-6.5, Hb-9.6, Platelets- 323	CA19.9-1454	USG guided	Head of pancreas	Adequate	Cohesive clusters and singly scattered	Present	Absent	Present	Neutrophils and lymphocytes	-	-	-	Neoplastic- Others- suggestive of pancreatic neuroendocrine tumor, Category-IV
69	1261249	TLC-7.2, Hb-10.2, Platelets-243	-	Endoscopic guided	Uncinate process of pancreas	Inadeqaute	-	Absent	Absent	Absent	Absent	-	-	-	Non Diagnostic-Category I
70	1276461	TLC-4.3, Hb-11.2, Platelets-200	CA19.9-1277	USG guided	Head of pancreas	Scantly cellular	Papillaroid clusters, tissue fragments and cohesive clusters	Present	Absent	Absent	Absent	-	Adenocarcinoma	-	Neoplastic, Others-Category IV, possibility of neoplastic mucinous cyst

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48

No. BFUHS/2K21p-TH/ 198 Date 6/1/2022

The Principal,
DMC, Ludhiana.

Subject: **Approval of Plan of Thesis.**

This is to inform you that the Faculty of Medical Sciences in its meeting held on 29.10.2021 has approved the plan of thesis of **Parul Verma**, a student of your college for **MD Pathology** along with the names of Supervisor/Co-Supervisor as under:-

Topic Plan of Thesis
Cytopathological spectrum of pancreatic lesions.

Supervisor
Dr. Pavneet Kaur Selhi
Prof.,
Dept. of Pathology,
DMCH, Ludhiana.

Co-Supervisor

Dr. Ruchita Tyagi
Asst. Prof.,
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Dr. Ramit Mahajan
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Dept. of Gastroenterology,
DMCH, Ludhiana.

The student has to submit the four copies of thesis (along with PDF format) , to the Controller of Examinations, BFUHS, Faridkot, at least six months before the commencement of theory examination, if he/she is otherwise eligible to take the examination. He /She must directed to attach a photocopy of this letter with the forwarding letter while submitting thesis to the University along with the letter of approval of University for change of supervisor/Co-Supervisor, change of topic,(if any).

Dr. S P Singh MS(Oph)
Controller of Examinations

Note :

99. If any discrepancy found regarding topic of thesis or Supervisor/Co-Supervisor, inform undersigned within one month after issue of this letter.

100. The student may submit the thesis as per the schedule already conveyed i.e for May/June examination 30th Nov of the preceding the year of examination and for Nov/Dec examinations 31st May of the year of examination.

CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS

THESIS PROPOSAL

FOR APPROVAL OF SUBJECT OF THESIS TO BE SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS

FOR THE DEGREE OF

MD

In

PATHOLOGY

OF THE

BABA FARID UNIVERSITY OF HEALTH SCIENCES

FARIDKOT

MARCH, 2021

Dr. Parul Verma

DEPARTMENT OF PATHOLOGY
DAYANAND MEDICAL COLLEGE AND HOSPITAL
LUDHIANA

ABSTRACT OF PLAN OF THESIS

Title	CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS
For the degree of	MD (PATHOLOGY)
Name of the candidate	Dr. Parul Verma
Supervisor	Dr. Pavneet Kaur Sehli, Professor, Department of Pathology, DMCH, Ludhiana
Co-supervisors	Dr. Ruchita Tyagi, Assistant Professor, Department of Pathology, DMCH, Ludhiana Dr. Ramit Mahajan, Associate Professor, Department of Gastroenetrology, DMCH, Ludhiana.
Institution	Dayanand Medical College and Hospital, Ludhiana
University	Baba Farid University of Health Sciences, Faridkot

Introduction: Pancreatic masses are a common cause of morbidity and mortality with non specific symptons. Management can be medical or surgical depending upon the site of involvement and etiology. Image guided FNAC has been increasingly utilized as a minimally invasive first line procedure for the diagnosis.

Aims & Objectives: To analyze cytomorphological features of pancreatic lesions and classify them according to Papanicolaou Society of Cytopathology System for reporting Pancreaticobiliary Cytology.

Material & Methods: Fine needle aspiration smears from pancreatic masses received in Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 2 years (one year retrospective, that is from 1st March 2020 to 28th February 2021 and one year prospective from 1st March 2021 to 28th February 2022) will be analyzed.

Clinical Significance: The smears obtained by FNAC (USG/CT/EUS guided) of pancreatic masses will be analysed and categorized on the basis of Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.

Keywords: Pancreatic, FNAC, Neoplastic, Papanicolaou, Malignant

(Signature)	(Signature)	(Signature)	(Signature)	(Signature)
Candidate	Co-supervisor	Co-supervisor	Supervisor	Principal

CERTIFICATE OF FACILITIES AVAILABLE

This is to certify that the facilities for work on the subject of thesis titled **"CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS"** exist in the Department of Pathology, DMC&H, Ludhiana and will be provided to the candidate. We will see that the data being included in the thesis is genuine and is collected by the candidate himself under our supervision and guidance.

Supervisor

Dr. Pavneet Kaur
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Place : Ludhiana

Date : 15th March 2021

APPROVAL PROFORMA
BY
RESEARCH & ETHICAL COMMITTEE
DAYANAND MEDICAL COLLEGE & HOSPITAL, LUDHIANA

Name of candidate	Dr. Parul Verma
Department	Pathology
Topic of Thesis	CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS
Likely date of appearing in PG examination	May 2023
Date of enrollment	26th June, 2020
Name of Head of Department	Dr. Harpreet Kaur
1) Supervisor **2) Co-Supervisors**	Dr. Pavneet Kaur Sehli Dr. Ruchita Tyagi, Dr. Ramit Mahajan
Signature of Members of Research Committee with Stamp	**Signature of Members of Ethics Committee with Stamp**
Dr. Harpreet Kaur (Professor & Head, Pathology)	Mr. R K Sharma (Legal Expert)
Dr. Jaspal Singh (Professor & Head, Surgery)	Dr. Ramit Mahajan (Associate Professor, Gastroenterology)
Dr. Dinesh Gupta (Professor & Head, Medicine)	Dr. Anu Sharma (Professor, Anatomy)
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Dr. Gurpreet S Wander (Vice Principal)	Dr. Gurpreet S Wander (Vice Principal & Professor & Head, Cardiology)
	Dr. Gagandeep Singh (Secretary, Ethics Committee Professor & Head, Neurology)

Approved: Yes / No

Dr. Sandeep Puri
Chairperson
Research Committee

Approved: Yes / ~~No~~

Prof. Arvind Malhotra
Chairperson
Ethics Committee

BABA FARID UNIVERSITY OF HEALTH SCIENCES, FARIDKOT
PROFORMA FOR REGISTRATION OF SUBJECT FOR DISSERTATION

1	NAME OF THE CANDIDATE AND ADDRESS	Dr. Parul Verma 342,C-2,B-1,Netaji Nagar, Salem Tabri, Ludhiana Punjab Pin-141008
2	NAME OF THE INSTITUTE	Dayanand Medical College and Hospital, Ludhiana
3	COURSE OF STUDY AND SUBJECT	MD Pathology
4	DATE OF ADMISSION OF COURSE	29-06-2020
5	TITLE OF THE TOPIC	CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS

6.0 BRIEF RESUME OF THE INTENDED WORK

6.1 NEED FOR THE STUDY

Pancreatic lesions are divided into benign and malignant. Among benign most common presentation is of acute and chronic pancreatitis and malignant lesion is mostly adenocarcinoma of pancreas. Pancreatic lesions both benign and malignant are a significant cause of morbidity and mortality. Malignant lesion mainly Adenocarcinoma of pancreas has become the third leading cause of death among cancers.[1] Hence the early detection and proper treatment whether it is medical treatment or surgical treatment for both benign and malignant lesions is of prime importance. This poor survival rate is mainly due to late clinical presentation, nonspecific signs and symptoms and other major drawbacks like limited diagnostics and limited therapeutic modalities. Accurate diagnosis of pancreatic lesions whether benign or malignant is important for improving the efficacy of the therapeutic interventions.[2] Pre-operative diagnosis of pancreatic masses is a challenging task owing to the non-specific clinico-radiological signs and technical difficulty in performing FNAC. FNAC can be performed by a gastroenterologist by endoscopic technique or by an interventional radiologist under CT/USG guidance. After performing FNAC, adequacy of the sample is checked so that proper outcome and diagnosis can be made by a cytopathologist. Benign lesions can be managed medically with proper follow ups whereas malignant lesions can be treated surgically. With the advent of advanced imaging techniques and guided FNA, cytology has emerged as a major tool for diagnosing pancreatic lesions, though surgical pathology is often considered to be the gold standard for diagnosis.[3] Endoscopic ultrasound-directed fine-needle aspiration is a minimally invasive technique for the biopsy of pancreatic cysts and mass lesions. The technique is associated with low morbidity and high diagnostic accuracy. Interpretation of cytologic material obtained from the pancreas is a challenging task due to many infectious diseases as well as benign and malignant neoplasms arising from the pancreas.[4] The cytologic appearances of a majority of

pancreatic neoplasms are of specific presentation, allowing precise recognition of the type of neoplasm present. Whereas separation of neuroendocrine, acinar, and ductal neoplasms is usually straightforward but the greatest diagnostic challenge in pancreatic fine-needle aspiration is the to distinguish between atypical epithelium secondary to chronic pancreatitis from well-differentiated ductal adenocarcinoma.[5] Also a number of in situ lesions have been identified recently which lead to complications in diagnosing pancreatic neoplasia on the basis of cytology which includes pancreatic intraepithelial neoplasia and intraductal papillary mucinous neoplasm.[6]

Moreover, FNAC of pancreatic masses allows for rapid on-site evaluation and triaging of material for ancillary studies. FNAC is a time saving, minimally invasive and well tolerated diagnostic modality which can be done as an out patient procedure to reach definitive diagnosis.[3]

Aspiration cytology and histology of pancreatic lesions together can provide a definitive diagnosis. Fine needle aspiration cytology (FNAC) can be done either under USG guidance or endoscopically and allows us to get samples not only for cytological evaluation but also for triaging material for ancillary studies such as flow cytometry, immunohistochemistry and molecular studies.[7]

Percutaneous punctures, USG and CT-guided approach for Fine needle aspiration has its own limitations as pancreas is a retroperitoneal organ which makes it probably inaccessible to reach and has close proximity to the other vital organs, therefore Endoscopic ultrasonography guided FNA is relatively safer and has low risk, leading to accuracy of the tissue biopsy.[7] Endoscopic ultrasonography (EUS) is an indispensable tool for diagnosing both solid and cystic pancreatic lesions.[8,9]

It has gained widespread acceptance among clinicians and patients. It provides useful information such as differentiating a neoplastic lesion from a non neoplastic one and further recognizing the lesion as benign or malignant. In this study, we have studied the entire spectrum of pancreatic lesions diagnosed on fine needle aspiration (FNA), which will throw light on pattern of lesions observed and has been

categorized according to the Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.[10]

6.2 REVIEW OF LITERATURE

Pancreas is a transversely oriented retroperitoneal structure extending from the C-loop of the duodenum to the hilum of spleen. It is a complex lobulated organ with distinct exocrine and endocrine components. The exocrine pancreas constitutes 80-85% of the organ and is composed of acinar cells and the endocrine part is 10-15% and is composed of islets of Langerhans.[1]

Inflammatory pancreatic lesions mainly present with pain in abdomen radiating to back which can be associated with nausea, vomiting and increase in serum amylase and lipase levels. Sensitivity of lipase is higher than amylase in diagnosing inflammatory lesions of pancreas though definitive diagnosis of any pancreatic lesion is through the FNAC.

Due to its retroperitoneal site, the imaging techniques are often required to guide the biopsy needle to sample the target area. Although clinical presentation, radiological findings and location of pancreatic mass is helpful, but tissue diagnosis remains the gold standard for final diagnosis and to plan the management. The diagnostic efficacy and accuracy of EUS guided FNA depends mainly on sample adequacy, lesion characteristics, endoscopy operator and cytopathology expertise.[11]

The neoplasm can be cystic or solid, while others can be benign or malignant. The endocrine tumors of pancreas are rare in comparison with tumors of exocrine pancreas, accounting for only 2% of all pancreatic lesions. Pancreatic cystic lesions comprises a vast group of lesions which posses varying degrees of malignancy out of which majority are pseudocysts and other are mucinous neoplasms which includes cystadenomas, mucinous cystadenocarcinomas, intraductal papillary mucinous neoplasms or serous cystadenoma.[12] Majority of tumors are seen in the head of the pancreas. The 5 year survival rate of pancreatic tumors is 10%.[1] As FNA is a minimally invasive technique, it helps investigators to get cyst fluid for biochemical and cytological evaluation.[12]

Distinction between neoplastic (benign and malignant) and inflammatory lesion is vital for patient management. The increasing use of radiological techniques has led to the identification of relatively small lesions, which can be accurately sampled with the help of image guidance.

The benefit of FNAC is simplicity of the procedure as it is less invasive and associated with fewer complications. It involves the use of endoscopic ultrasound in which an echoendoscope is placed into the stomach or duodenum and by the use of ultrasound transducer on the tip of echoendoscope, a small gauge needle is passed into the lesion. FNA can be done through transgastric route if the lesion is in pancreatic tail or body as they are close to stomach bed, or through transduodenal route if the lesion is in pancreatic head.[13]

FNAC sometimes has its own limitations to reach a final diagnosis therefore cell block technique is useful and improves the efficacy and accuracy of cytological diagnosis. Cell block technique allows processing of limited amount of cellular material for histopathological analysis, cytochemistry and limited IHC.[14] Thus the combination of cytological smears, cell block preparation with panel of special stains optimizes the utility of FNAC in the diagnosis of pancreatic lesions.[14]

Cytology of Pancreatic Masses**-**

Aspirates from the pancreas is divided into neoplastic and non neoplastic lesions. Neoplastic lesions are further divided into benign and malignant categories while non neoplastic lesions can be inflammatory or non inflammatory.[15-17]

Common lesions of pancreas include-

1- Non neoplastic lesions: Pancreatitis (Acute, Subacute and chronic), Pseudocysts and cysts.
2- Neoplastic lesions: Cystadenoma, Pancreatic carcinoma (ductal cell origin and acinar cell orogin), cystadenocarcinoma, solid papillary neoplasm, islet cell tumour and metastasis to pancreas.

Endoscopic ultrasound—guided fine-needle aspiration (EUS-FNA) is first-line procedure in diagnosing the solid pancreatic lesions. Of the broad differential diagnosis of solid pancreatic masses including both malignant and benign lesions, the primary ductal adenocarcinoma accounts for atleast 85% of solid pancreatic masses, being the most common of them.[18,19]

Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology has divided lesions of pancreas into**:**[20]

1. **Non Diagnostic**
2. **Negative for malignancy**

Benign pancreatic tissue

Acute pancreatitis

Chronic pancreatitis

Autoimmune pancreatitis

Pseudocyst

Lymphoepithelial cyst

Spenule/ accessory spleen

3. Atypical

4. Neoplastic

Benign: Serous cystadenoma

Neuroendocrine microadenoma

Lymphangioma

Other: Well differentiated neuroendocrine tumor

Intraductal papillary mucinous neoplasm, all grades of dysplasia

Mucinous cystic neoplasm

Solid pseudopapillary epithelial neoplasm

5-Suspicious (for malignancy)

6- Positive for malignancy

Ductal adenocarcinoma of the pancreas and its variants

Cholangiocarcinoma

Acinar cell carcinoma

Poorly differentiated (small and large cell) neuroendocrine carcinoma

Pancreatoblastoma

Lymphoma

Metastatic malignancy

WHO CLASSIFICATION [21]

Benign epithelial tumours and precursors

Serous cystadenoma NOS

Macrocystic (oligocystic) serous cystadenoma

Solid serous adenoma

Von Hippel-Lindau syndrome-associated serous cystic neoplasm

Mixed serous-neuroendocrine neoplasm

Serous cystadenocarcinoma NOS

Glandular intraepithelial neoplasia, low grade

Glandular intraepithelial neoplasia, high grade

Intraductal papillary mucinous neoplasm with low grade dysplasia

Intraductal papillary mucinous neoplasm with high grade dysplasia

Intraductal papillary mucinous neoplasm with associated invasive carcinoma

Intraductal oncocytic papillary neoplasm NOS

Intraductal oncocytic papillary neoplasm with associated invasive carcinoma

Intraductal tubulopapillary neoplasm

Intraductal papillary neoplasm with associated invasive carcinoma

Mucinous cystic neoplasm with low grade dysplasia

Mucinous cystic neoplasm with high grade dysplasia

Mucinous cystic neoplasm with lassociated invasive carcinoma

Malignant epithelial tumours

Duct adenocarcinoma NOS

Colloid carcinoma

Poorly cohesive carcinoma

Signet ring cell carcinoma

Medullary carcinoma NOS

Adenosquamous carcinoma

Hepatoid carcinoma

Large cell carcinoma with rhabdoid phenotype

Carcinoma , undifferentiated ,NOS

Undifferentiated carcinoma with osteoclast like giant cells

Acinar cell carcinoma

Acinar cell cystadenocarcinoma

Mixed acinar neuroendocrine carcinoma

Mixed acinar endocrine ductal carcinoma

Mixed acinar ductal carcinoma

Pancreatoblastoma

Solid pseudopapillary neoplasm of pancreas

Solid pseudopapillary neoplasm with high grade carcinoma

Pancreatic neuroendocrine microadenoma

Neuroendocrine tumour NOS

Neuroendocrine tumour, grade 1

Neuroendocrine tumour, grade 2

Neuroendocrine tumour, grade 3

Pancreatic neuroendocrine tumour, non functioning

Oncocytic neuroendocrine tumour, non functioning pancreatic

Pleomorphic neuroendocrine tumour, non functioning pancreatic

Clear cell neuroendocrine tumour, non functioning pancreatic

Cystic neuroendocrine tumour, non functioning pancreatic

Functioning pancreatic neuroendocrine tumours

Insulinoma

Gastrinoma

VIPoma

Glucagonoma

Somatostatinoma

ACTH producing tumour

Enterochromaffin cell carcinoid

Serotonin producing tumour

Neuroendocrine carcinoma NOS

Large cell neuroendocrine carcinoma

Small cell neuroendocrine carcinoma

Mixed neuroendocrine non neuroendocrine neoplasm (MiNEN)

Mixed acinar endocrine carcinoma

Mixed acinar neuroendocrine carcinoma

Mixed acinar endocrine ductal carcinoma

6.3 AIMS AND OBJECTIVES OF THE STUDY

To analyze cytomorphological features of pancreatic lesions and classify them according to Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.

7. MATERIALS AND METHODS

7.1 SOURCE OF DATA

Fine needle aspiration smears from pancreatic masses received in Department of Pathology of Dayanand Medical College and Hospital, Ludhiana over a period of 2 years (one year retrospective, that is from 1st March 2020 to 28th February 2021 and one year prospective from 1st March 2021 to 28th February 2022) will be analyzed.

7.2 METHOD OF COLLECTION OF DATA

INCLUSION CRITERIA

FNAC samples from pancreatic masses received in the Cytology Laboratory of the Pathology Department which will include.

1- FNAC slides received after guided aspiration (USG/CT or endoscopic ultrasonography).

2- Prepared and stained slides for review from outside centre.

EXCLUSION CRITERIA

Samples obtained from lesions other than pancreas.

PROCEDURE

After informed consent, radiologically and EUS guided FNAC will be done using 23 gauge needle attached to 20cc disposable plastic syringe under aseptic conditions. Under the radiological guidance, aspiration will be performed and slides will be prepared immediately. One of the slide will be utilized for rapid on the site evaluation for adequacy of the sample received after staining with Toulidine Blue. Two slides will be wet fixed in 95% ethanol for Papanicolaou stain and Hematoxylin and Eosin stain. The remaining smears will be air dried and stained by May Grunwald Geimsa stain. FNA samples collected in separate pass will be fixed in 10% formalin, processed and embedded to make cell blocks. Sections will be stained by H&E stain. Special stains will be done whenever necessary.

DURATION OF STUDY

Prospective- 1 Year, 1st March 2021 to 28th Feb 2022

Retrospective- 1 Year, 1st March 2020 to 28th Feb 2021

STUDY DESIGN

This is both retrospective and prospective study.

OUTCOME

The smears obtained by FNAC (USG/CT/EUS guided) of pancreatic masses will be analysed and categorized on the basis of Papanicolaou society of cytopathology system for reporting pancreaticobiliary cytology.

7.3 DOES THE STUDY REQUIRE ANY INVESTIGATIONS OR INTERVENTIONS TO BE CONDUCTED ON PATIENTS OR OTHER HUMANS OR ANIMALS? IF SO, PLEASE DESCRIBE BRIEFLY.

No

7.4 HAS ETHICAL CLEARANCE BEEN OBTAINED FROM YOUR INSTITUTION IN CASE OF 7.3?

Attached herewith

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PROFORMA

Serial no.- Asp. No Date-

Name Age Sex

MRD No. Phone No.

Address

Clinical features with duration-

Past history of cancer or chemotherapy-

Clinical diagnosis-

Personal History-

-Alchohol -Smoking -Other

Clinical Examination:

- Pallor
- Icterus
- Lymphadenopathy

Radiological findings Site Size

Solid Mass

Cystic Mass

Calcification

Investigations-

S.Calcium Triglycerides

Serum Tumor Marker (CEA) Cholestrol

Signature of Candidate **Signature of Supervisor**

Serum Tumor Marker (CA 19-9)

Amylase Lipase

Cyst Fluid (Amylase) Cyst Fluid (Lipase)

Cyst Fluid (CEA)

Testing for TB-Mantoux, AFB smear

Sample adequacy- Yes/No

- Number of passes-

FNAC Findings:

-Cellularity –

-Architectural Pattern-

-N:C ratio -Necrosis

-Nuclei -Granuloma

-Nucleoli -Inflammatory cells-

-Cytoplasm -Foamy Macrophages

-Giant Cells

Special Stains -PAS -GMS -Others

Cytopathological Diagnosis:

Histopathological Diagnosis:

IHC (If any)

Final Diagnosis

Signature of Candidate **Signature of Supervisor**

INFORMED PATIENT CONSENT

Date: _____

I.....D/o, W/o,
S/o..... .....am willing to participate in the study **"CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS"** The procedure with its complications has been explained to me in local vernacular language. I have fully understood that no special tests and extra expenditure in any form, merely for the purpose of thesis is being carried out. I am free to opt out the study any time without assigning any reason.

.....
Signature of the Witness

.....
Signature of the patient

Name:

Signature of Supervisor

Signature of Candidate

मरीज अनुमति फार्म

तिथि _____

मैं _____पत्नी/पुत्र/पुत्री _____ निवासी _____ इस शोधकार्य **"CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS"** में भाग लेने के लिए सहमत हूँ। मैं इस शोधकार्य में भाग लेने के लिए अपनी स्वेच्छा से तैयार हूँ। मैं पुष्टि करता/करती हूँ की यह स्वीकृति देने के लिए मुझे कोई आर्थिक प्रलोभन नहीं दिया गया और न ही दबाव डाला गया है। मुझे इस शोधकार्य का उद्देश्य स्पष्ट कर दिया गया है और मुझे यह विश्वास है की यह विज्ञान और मानवता के लाभ के लिए है। मुझे इस शोधकार्य में होने वाले जोखिम के बारे में समझा दिया गया है और मेरी समझ में यह जोखिम बहुत मामुली है।

मैं इस शोधकार्य में भाग लेने के सम्बन्ध में किसी भी समय अपनी अस्वीकृति व्यक्त कर सकता/सकती हूँ और मेरे अस्वीकृति व्यक्त करने का मेरे इलाज पर कोई प्रभाव नहीं पड़ेगा।

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गवाह के हस्ताक्षर रोगी के हस्ताक्षर/अंगूठे का निशान

नाम: नाम:

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अन्वेषक के हस्ताक्षर

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विद्यार्थी के हस्ताक्षर

ਮਰੀਜ਼ ਰਜ਼ਾਮੰਦੀ ਫਾਰਮ

ਮਿਤੀ_____

ਮੈ_____ਪਤਨੀ/ਪੁੱਤਰ/ਪੁੱਤਰੀ_____ਵਾਸੀ

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"CYTOPATHOLOGICAL SPECTRUM OF PANCREATIC LESIONS" ਤੇ ਚਲ ਰਹੀ ਖੋਜ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਰਜ਼ਾਮੰਦ ਹਾਂ। ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਲਈ ਮੈ ਆਪਣੀ ਮਰਜ਼ੀ ਨਾਲ ਤਿਆਰ ਹਾਂ। ਮੈ ਇਹ ਦਸਣਾ ਚਾਹੁੰਦਾ ਹਾਂ/ ਚਾਹੁੰਦੀ ਹਾਂ ਕੇ ਇਹ ਰਜ਼ਾਮੰਦੀ ਦੇਣ ਵਾਸਤੇ ਮੈਨੂ ਕਿਸੇ ਵੀ ਤਰਾਂ ਦਾ ਲੋਭ-ਲਾਲਚ ਨਹੀ ਦਿੱਤਾ ਗਿਆ ਅਤੇ ਨਾ ਹੀ ਕੋਈ ਦਬਾ ਪਾਇਆ ਗਿਆ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਦਾ ਮਨੋਰਥ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਭਰੋਸਾ ਦਵਾਇਆ ਗਿਆ ਹੈ ਕੇ ਇਹ ਖੋਜ ਵਿਗਿਆਨ ਅਤੇ ਮਾਨਵਤਾ ਦੀ ਭਲਾਈ ਲਈ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਵਿਚ ਹੋਣ ਵਾਲੇ ਖਤਰੇ ਬਾਰੇ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ ਅਤੇ ਮੈਨੂ ਇਹ ਯਕੀਨ ਹੈ ਕੇ ਇਹ ਖਤਰਾ ਬਹੁਤ ਮਾਮੂਲੀ ਹੈ। ਮੈਨੂ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਦਾ ਢੰਗ – ਤਰੀਕਾ ਸਮਝਾ ਦਿੱਤਾ ਗਿਆ ਹੈ।

ਮੈ ਇਸ ਖੋਜ ਕੰਮ ਵਿਚ ਹਿੱਸਾ ਲੈਣ ਬਾਰੇ ਆਪਣੀ ਰਜ਼ਾਮੰਦੀ ਕਿਸੇ ਵੀ ਸਮੇ ਵਾਪਸ ਲੈ ਸਕਦਾ ਹਾਂ/ ਸਕਦੀ ਹਾਂ ਅਤੇ ਮੇਰੀ ਰਜ਼ਾਮੰਦੀ ਵਾਪਸ ਲੈਣ ਦਾ ਮੇਰੇ ਇਲਾਜ ਤੇ ਕੋਈ ਅਸਰ ਨਹੀ ਹੋਵੇਗਾ।

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ਗਵਾਹ ਦੇ ਹਸਤਾਖਰ ਮਰੀਜ਼ ਦੇ ਹਸਤਾਖਰ

ਮਿਤੀ_____ ਮਿਤੀ_____

ਪਤਾ _____ ਪਤਾ _____

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ਨਿਰੀਖਕ ਦੇ ਹਸਤਾਖਰ

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ਸਿਖਿਆਰਥੀ ਦੇ ਹਸਤਾਖਰ